COMPARING THE ACCURACY OF SURVIVAL PREDICTION WITH TWO DIFFERENT PROGNOSTIC SCORING SYSTEMS, IN INDIAN CANCER PATIENTS RECEIVING PALLIATIVE CARE/PALLIATIVE RADIOTHERAPY

DISSERTATION SUBMITTED IN PARTIAL FULLFILLMENT OF THE REQUIREMENT FOR THE AWARD OF THE MD DEGREE (BRANCH –IX) IN RADIOTHERAPY OF THE TAMILNADU DR. M.G.R MEDICAL UNIVERSITY EXAMINATION TO BE HELD IN MARCH 2010

CERTIFICATE

This is to cerfify that the thesis entitled **"Comparing the accuracy of survival prediction with two different prognostic scoring systems,in Indian cancer patients receiving palliative care and/or palliative radiotherapy"** submitted by **Dr.Abraham Samuel** in part of fulfillment of the MD branch (IX) Radiotherapy degree examination of the Tamilnadu Dr.M.G.R Medical university Chennai,to be held in March 2010 is a bonafide work done by him under guidance of Dr.Reena Mary George, Professor, Christian Medical College Vellore.

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ACKNOWLEDGEMENTS

I am extremely to grateful to Dr. Reena Mary George Professor and Head of Palliative Medicine for helping me in selecting this topic ,for helping me generously through out the course of this study ,for all the support and being my guide.

I express my gratitude to Dr Subhashini John, Professor and head of Radiotherapy for her guidance and support.

I am also grateful to Dr.PN Vishwanathan for support and valuable advices.

I am grateful to the patients and their families for helping me by participating in this study.

I am thankful to Mr. Ramu, social worker in Palliative Medicine for data managing and following up the palliative care cohort. and the entire palliative care team.

I wish to express sincere thanks my fellow registrars, radiographers in the radiotherapy department for all the help.

I am thankful to God for giving me good health and wisdom in my day to day life.

CONTENTS

AIM OF THE STUDY

To evaluate the Palliative Prognostic Score (Pap)and the Palliative Prognostic Index (PPI) in patients receiving palliative radiotherapy and /or palliative care.

Primary Objective

To compare the sensitivity, specificity and positive predictive values of the two scales in prognosticating 1 week, one month, and three month survivals. The primary outcome was sensitivity and specificity for estimating 1 month survival.

Secondary objectives

1. 1.To document the median survivals of patients classified into good, intermediate, and better prognostic categories.

2. To assess the sensitivity and specificity of Score B when clinician's prediction of survival is added to the score (modified score B). (Is modified score B better than the original score B?)

3. To assess the sensitivity and specificity of score A when laboratory tests are excluded from the scoring system (How accurate is a simpler score A?)

INTRODUCTION

Physicians who are taking care of terminally ill patients are often confronted with a question like “Doctor, How long do i have?” from the patients . Prognostic information is important with regards to continuation of treatment which associated with further morbidity ,financial burden to care takers,place of care ,timely referral to hospice or palliative care center,to mentally and spiritually prepare for an imminent death,other family and social commitments.

Accurate prediction of survival is necessary for clinical, organizational, and ethical reasons, in helping to avoid inappropriate therapies in vulnerable patients and, in providing appropriate interventions where there is likelihood of benefit. Patients and their families often request such information so that they can make treatment choices and set personal goals.

If patients can be reliably identified who will die in the next few days irrespective of what is done to them, then burdensome, ineffective overtreatment maybe avoidable. Likewise, undertreatment due to therapeutic nihilism in those with a good chance of survival may also be prevented [1]. The steering committee of the European Association for Palliative Care stated that prognostication of life expectancy is a significant clinical commitment for clinicians involved in oncology and palliative care and can be achieved by combining clinical experience and evidence from the literature. The committee recommended that using and communicating prognostic information should be part of a multidisciplinary palliative care approach. [2]

REVIEW OF LITERATURE

CLINICIAN'S PREDICTION OF SURVIVAL (CPS).

CPS is clinician's estmate of the probable life expectancy of the patients based on his or her experience. However, reports on its accuracy are conflicting, literatures has been demonstrated that the CPS can be considerably inaccurate and physicians are systematically over optimistic in their assessments- for example in a study the median clinician estimated survival was 75 days, but the median actual survival was 25 days [3]. The experience and specialty of the physician and the nature of the physician–patient relationship may be confounders for the accuracy of the CPS .A prospective study of CPS when making referrals to a U.S. hospice indicated academic oncologists were more accurate than community oncologists or family physicians; and more experienced physicians were more accurate. However, this increased accuracy was blunted if the relationship between the physician and patient was strong. This led the authors to suggest an experienced but uninvolved specialist physician was likely to be the most accurate and might be requested for a prognostic 'second opinion' if an accurate prognosis was deemed essential (e.g., deciding to withdraw life sustaining treatment) [4]. Conversely, Oxenham in a study on hospice patients reported that predicting survival in the last days of life needs a close knowledge about patients which are easily gained by spending time with them rather than depending solely on lab investigations.The accuracy in predicting survival improves over a period as there is increase in knowledge regarding patients condition .In the later stage accuracy of the clinician was improved and among the staff the nursing auxillaries were most

accurate in predicting the prognosis as they spend considerable time with the patients [5].

In a systematic review Glare et all found that the temporal CPS overestimated the actual survival (AS) by 45% near to with in 1 week in only 25% cases.But there was good correlation [6]. In a systematic review by Vigano et al the CPS proved to be predictive of the Actual Survival (AS) even though the magnitude of the association was low [7],[8],[9],[10],[11]. In a study by Vigano A on 227 consecutive patients, the CPS was a strong, independent prognostic value at multivariate analysis [12].In a Canadian study the specificity of the CPS for less than equal to 2 months,2-6 months and more than 6 months were 95%,51% and 81% respectively.But the sensitivity was 31%,68% and 54% respectively. The positive predictive values (PPV) were 74%,41%,60% and negative predictive values (NPV)were 75%,76% and 77% respectively.In this study there was high specificity for the first and third categories[13]. In a review of CPS characteristics based on five studies, estimated survival was higher than AS by a factor ranging from 1.2 to 4, with a percentage of error between 30% and 78% and a rate of optimistic errors out of the total errors of 63% to 92% [12].

A study done by Christakis et al found that only 20% of predictions were correct, with doctors overestimating survival by a factor of 5.3. This lower prognostic accuracy was correlated with a longer doctor–patient relationship and a shorter time interval since last examination. The other reasons could be ignorance of prognostic factors, refusal to accept that patient is in the terminal stage of disease, optimistic prejudice, and a feeling of omnipotence [4].In a study by Maltoni etal with experienced oncologists, the CPS had a percentage of error of only 30%, with a good balance between

overoptimistic and overpessimistic errors. The CPS obtained a higher prediction accuracy than reported in earlier studies (correlation coefficient with actual survival = 0.51) and than that obtained with KPS alone (correlation coefficient = 0.37)[10]. The CPS is a useful base for a prognostic estimate even though as a subjective estimate it is influenced by the doctor's experience and could be poorly reproducible and unsuitable for non palliative physicians and medical program managers [14].

Two ways of improving the CPS have been suggested [15].

1. Asking care givers not previously involved with the patient to estimate survival to overcome optimistic proclivity, in that survival predictions averaged across physicians are more accurate .

2. Integration of the CPS with more objective and reproducible survival predictors that have emerged from multivariate analysis [15].

Some studies shows that KPS has greater prognostic capability [16]. The modifications of the KPS have proved capable of a prognostic impact in a palliative setting: Palliative Performance Scale [17].The Performance Status has also shown a prognostic capacity in groups of patients eligible for phase I studies with advanced or metastatic cancer [18,19]. The KPS showed an increase in its prognostic capacity when integrated with data concerning the presence of specific symptoms.KPS is a reliable tool to predict the the imminent death if is less than or equal to 40. But also a high score does not mean a long survival. The clinical prediction of survival is more accurate than KPS in estimating the life span of patients with advanced malignancy.In the study by Maltoni et al in 100 patients the CPS obtained a higher prediction accuracy

than the past studies with a correlation coefficient with actual survival=0.51 and that obtained with KPS alone; correlation coefficient =0.37.The median difference between predicted and expected survival was only 1 week[10].

PAP SCORE

A study by Marco Pirovano et al showed the construction of a simple prognostic score based on factors identified in a prospective multicenter study done in 22 centres in Italy. There were 519 patients with a median survival of 32 days who were diagnosed to have advanced solid tumours and were no longer considered suitable for primary treatment. They used an exponential multiple regression model and from an initial model with 36 variables, a final model was created by means of a backward selection procedure. There are six variables are found to be independent predictors of survival: Clinical Prediction of Survival (CPS), Karnofsky Performance Status (KPS), anorexia, dyspnea, total white blood count (WBC) and lymphocyte percentage.

These variables were given a numerical score, based on the relative weight of the independent prognostic significance shown by each single category in the multivariate analysis. The sum of the single scores gives the overall PaP Score for each patient and it ranges from 0 to 17.5 .It can subdivide the study population into three groups, each with a different probability of survival at 30 days: (1) group A: probability of survival at 30 days >70%, with patient score less than equal to 5.5; (2) group B: probability of survival at 30 days 30–70%, with patient score 5.6–11.0; and (3) group C: probability of survival at 30 days <30%, with patient score >11.0.Using this method,

178/519 (34.3%) patients were classified in risk group A, 205 (39.5%) patients were in risk group B, and 136 (26.2%) patients were in risk group C. The patients classified in the three risk groups had a very different survival experience (logrank=294.8,P<0.001), with a median survival of 64 days for group A, 32 days for group B, and 11days for group C. The PaP Score based on these simple variables were proved to be statistically significant in a multivariate analysis [8].

A prospective study was conducted in Australia by Glare et al to validate PaP score. They calculated individual PaP scores for 100 terminally ill patients (91% with known malignant disease and 9% with Non-cancer diagnosis).This was done in a palliative medicine consultation service based in a university teaching hospital.The PaP score was able to subdivide this patient population into 3 groups (A,B,C).The percentage survival at 30 days for the three groups were 66%,54%, and 5% respectively. These results showed that PaP was good at predicting the survival for the poorest survival group ;but less at distinguishing between the good and intermediate groups.

The PaP score depends on clinical prediction of survival (CPS) and this is a weakness of the PaP model.Major variations occur among the clinicians based on their experience and knowledge in the care of terminally ill patients. The ability is derived from the integration of other clinical data like knowledge of the natural history of disease, rate of progression, response to treatment, comorbidities and psychological issues. But CPS has unique role in PaP score in estimating the survival [1].

In another study by Glare et al the PaP score was validated in 100 patients with advanced cancer under the care of a medical or radiation oncologist at a university teaching hospital in Australia.

They used survival data from 98 patients. The overall median survival was 12 weeks (interquartile range, 7 to 25 weeks). The PaP score divided the heterogeneous patient sample into three isoprognostic groups related to the chance of surviving 1 month, with 64 patients in group A (> 70% chance), 32 patients in group B (30% to 70% chance), and four patients in group C (< 30% chance). The estimated median survival of the three groups was 17 weeks (95% CI, 12 to 26 weeks), 7 weeks (95% CI, 4 to 12 weeks), and less than 1 week (95% CI, < 1 to 3 weeks), respectively. These survival differences were highly significant (log-rank test of trend, 12 = 25.65; P < .0001). The 1-month survival of the groups was 97%, 59%, and 25%, respectively [20].

In a study by Maltoni PaP score was calculated for 451 patients in an Italian palliative care program. A scoring was given and patients are subdivided into 3 specific risk groups based on the PaP risk variables. There was a training group and testing group.The median survival was 76 days in group A(with a 86.6 % probability of 30-day survival,32 days in group B(with a 51.6% probability of 30 day survival), and 14 days in group C (with a 16.9% probability of 30 day survival). The survival medians for the trainset was also similar (64 days in group A, 32 days in groupB,and 11 days in groupC)[21].

In a study by Davide et al the PaP score was applied to 173 patients with advanced, pretreated gastrointestinal or nonsmall cell lung cancer before starting a

further line of palliative chemotherapy . Univariate and multivariate analysis of survival was performed using the logrank test, the Cox regression model respectively. Symptom distress scores were compared using multivariate analysis of variance test for repeated measures, and overall symptom distress score was compared using analysis of variance test for repeated measures. The overall median survival was 26 weeks; in PaP score class A it was 32 weeks, and in class B 8 weeks ($p<0.0001$). No patient was classified in class C. The two-class PaP score resulted in an independent prognostic factor ($p=0.022$), as well as Karnofsky performance status ($p=0.002$)and colorectal cancer ($p=0.017$). A trend towards worsening of symptom distress was observed in the entire population and in class A. It showed that the PaP score can predict patients who could benefit by palliative chemotherapy from those who benefit by supportive and palliative care. But the data were insufficient to validate the use of the PaP score in patients to be treated with palliative chemotherapy. They advised further trials to validate the usefullnes of PaP in this setting of selecting patients for palliative chemotherapy [22].

PALLIATIVE PROGNOSTIC INDEX

Morita et al analysed the data on performance status and the presence or absence of 21 symptoms in 150 patients admitted in a hospice .They identified 5 variables like performance status, oral intake ,oedema, dyspnoea at rest and delirium as independent predictors of survival and each variable are given a partial score. A sum of the partial scores of these variable ranged from 0 to 15.The patients were grouped in to three depending on their PPI score(group A,PPI less than or equal to 2;group B more than 2but less than 4;group C with a PPI of more than 4).Using the

score >4 was taken as a cut-off ,a 6 week survival was predicted with a positive predictive value of 0.86 and a negative predictive value of 0.70.This PPI was then tested in an Independent cohort of 95 patients and the predictive value of the scoring system was confirmed, for patients with a PPI score >4,6 week survival was predicted with PPV of 0.83 and NPV of 0.71[23].

In another study by Morita et al by 2 independent series of of hospice patients were studied(n= 150 and 108).He studied whether clinical prediction of survival (CPS) can be improved using PPI . In the first study, the CPS was prospectively recorded by primary physicians on the basis of their clinical experiences. In the second study, physicians estimated patient prognoses with a reference to the PPI score. The cases where the differences between actual survival (AS) and CPS were 28 days or longer significantly decreased in the second study compared to the first study (42% vs 23%, P < 0.01). Also, the cases where AS was either twice longer or half shorter than CPS significantly declined (49% vs 37%, P= 0.050).). As well, serious errors, defined as the cases where AS was either (a) 28 days and twice longer than CPS or (b) 28 days and half shorter than CPS, were also significantly decreased from 27% in the first study group to 16% in the second study group (P = 0.028).The PPI was found to predict 6 week survival with a PPV of 0.91 and NPV of 0.67[24, 25]. In another study by Stone et al PPI was validated .The study population included patients receiving palliative chemotherapy and radiotherapy.The patients were included in a hospital –based consultancy palliative care service , a hospice home care service and a hospice inpatient unit. There were a total of 194 patients and 43% of the patients were receiving chemotherapy/or radiotherapy or both. The patients were divided into 3 risk

groups based on the PPI score.Group I corresponded to PPI less than or equal to4,median survival was 68 days(95% confidence interval[CI]52,115 days).Group 2 corresponded to those with PPI more than 4 but less than equal to 6,median survival was 21 days(95% CI 13,33), and group 3 corresponded to patients with PPI more than 6 ,median survival was 5 days(95% CI 3,11).In this study survival of less than 3 weeks was predicted with a positive predictive value of 86% and negative predictive value of 76 %.Survival less than 6 weeks was predicted with a positive predictive value of 91% and negative predictive value of 64%.The PPI was quick and easy to use and it can be applied in hospital based,home based or hospice based patients [26].

In a recent study from Germany by Stiel et al PPI, PaP-S and physicians' estimations were compared in survival predictions in 83 patients. The correlations between survival time and the prognostic scores or physicians' prognosis were lower. The physicians' estimations overestimated survival time on average fourfold. The estimations were more or less correct for the good and bad prognosis groups. None of the prognostic scores could show a precise reliable prognostic estimate for the individual patient. But scores were helpful for ethical decision making and team discussions. They opine that estimating survival time from clinical experience seems to be easier and practical in the 2 extreme groups (very good vs very bad prognosis).The limitation of this study was its small sample size (83) patients [27].

MATERIALS AND METHODS

This was an observational cohort study done in patients receiving palliative radiotherapy. Concurrently a second cohort was followed up by the palliative care team, in the palliative care service.

Inclusion Criteria

- All patients receiving palliative radiotherapy.

Exclusion Criteria

- Patients less than eighteen years of age.
- Patients or families who decline to participate.
- Cases where a suitable informant could not be identified .
- Cases where language or other barriers prevent adequate monthly telephone/postal/ clinic follow up.

Pap Versus PPI

Patients with incurable cancer who are receiving palliative radiotherapy were clinically assessed and scored at baseline using both the Palliative Prognostic Scale (PaP) and the Palliative Prognostic Index (PPI). The scoring systems classified patients into poor, intermediate or better prognostic groups at baseline. These scoring systems were based on the presence of symptoms such as dyspnoea, anorexia, oedema, the general performance status. A family member or contact person was contacted once a

month to enquire about the patient's condition. Survival or date of death was noted based on this information. This enabled us to know which patients have survived less than 1 week, 1 month or three months. The survival data thus obtained, was compared with the baseline categorization to assess and compare the sensitivity, specificity and positive predictive values of the PaP and the PPI.

PaP(Palliative Prognostic Score). PaP is a scoring system developed to estimate the survival of terminally ill cancer patients. It was constructed by adding six variables which were individually predictors of survival. These variables were clinician prediction of survival, Karnofsky performance status, anorexia, dyspnoea, total white blood count and lymphocyte percentage. Patients who have not had a WBC count in the past two weeks will have a blood test done The PaP score is generated by applying a 'weighted' scoring system to each of these variables. Total scores range from 0 to 17.5 and patients were divided into three prognostic categories. The total scores for the three groups A,B,C were 0-5.5,5.6 -11,11.1-17.5 and the 30 days survival probabilities were >70%,30–70%,<30% respectively.

PAP SCORE

Score	Prognostic variable							
0	Dyspnoea Absent							
1	Present							
0	Anorexia Absent							
1.5	Present							
0	Karnofsky performance status ≥ 50							
2.5	10-40							
0	Clinician Prediction of Survival (weeks) >12							
2	11-12							
2.5	7-10							
4.5	5-6							
6	3-4							
8.5	1-2							
0	Total white blood cell count Normal(4800-8500) cell/mm^3							
0.5	High (850-11 000) cell/mm^3							
1.5	Very high (>11 000) cell/mm^3							
0	Lymphocyte percentage Normal (20%-40%)							
1	Low (12%-19.9%)							
2.5	Very low (0%-11.9%)							

Interpretation of the PaP score

Risk group	Total score
A	0-5.5
B	5.6-11
C	11.1-17.5

PPI (PALLIATIVE PROGNOSTIC INDEX).

Morita et al developed PPI based on five variables like performance status, oral intake, oedema, dyspnoea at rest and delirium which were independently predictive of survival and each of these variables had a partial score (two or three).The total PPI score is calculated from the sum of the partialscores and could range from 0 to 15 and patients were divided in to three groups A,B,C with scores less than or equal to 4,more than 4 but less than or equal to 6,more than 6 respectively.Total score of 4 was taken as a cut off and positive predictive value (PPV) for 6-week survival and negative predictive value (NPV) for 6-week survivals were 0.83, 0.71 respectively.

.Score	Variable								
4	Palliative performance scale (modified Karnofsky) 10-20								
2.5	30-50								
0	≥60								
2.5	Oral intake Severely reduced								
1.0	Moderately reduced								
0	Normal								
1.0	Oedema Present								
0.0	Absent								
3.5	Dyspnoea at rest Present								
0.0	Absent								
4.0	Delirium Present								
0.0	Absent								

Risk Group	Total score
A	<\=4
B	> 4 and < or = 6
C	> 6

Modified PaP (MPaP) Score

It was created by removing the blood investigations (total white blood cell and differential lymphocytes counts) scores from the original PaP score.

In this there were 3 categories A,B,C with scores in the range of 0 to 5,5.1 to 7 and 7.1 to 13.5 respectively.

Modified PPI (MPPI) Score

It was created by adding the partial score of Clinician Estimated Survival (CPS) to the original PPI score.The 3 new categories A,B,C with scores in the range of 0 to 6,more than 6 to less than 11 and more than or equal to 11 respectively.

Ethics approval

The study was presented to the Institutional Review Board of the Christian Medical College, Vellore. 18.12.2008 and No.6728. Data collection was started after IRB approval was obtained.

Consent

All patients were explained about the study, the follow up and informed consent was obtained.

Patients were recruited in the study from January 2009 to September 2009. Relatives were contacted regularly by telephone to document survival or date of death.

Statistical analysis

The dataset was analyzed using SPSS version 16.0. The results of the cohort followed up in Palliative Care are also reported here with permission.

The cohorts were analyzed individually and together, to document the sensitivity, specificity, and positive predictive values of the original and modified PaP and PPI scores, in predicting I month and three month survival. This information was used to ascertain if any particular prognostic score was clearly superior in predicting survival.

A) Sensitivity

The sensitivity of a diagnostic test is the proportion of patients for whom the outcome is positive that are correctly identified by the test or the ability of a test to identify correctly all those who have the disease (true positives).

Sensitivity = True positive/ (True positive +False negative) x 100.

B) Specificity

The specificity is the proportion of patients for whom the outcome is negative that are correctly identified by the test or the ability of a test to identify correctly those who do not have the disease (true negatives).

Specificity =True negative /(True negative+False positive) x100.

C) Positive Predictive Value (PPV):

The positive predictive value (PPV) of a test is the probability that a patient has a positive outcome given that they have a positive test result. This is in contrast to sensitivity, which is the probability that a patient has a positive test result given that they have a positive outcome.

PPV=True positive/ (True positive +False positive) x 100.

D) Negative Pre dictive Value (NPV): The negative predictive value (NPV) is the probability that a patient has a negative outcome given that they have a negative test result, in contrast to specificity, which is the probability that a patient has a negative test result given that they have a negative outcome[28,29]

NPV= True negative /(True negative+False negative) x100.

Example:

The PPV of the test using lactate level above 1.5 mmol/l as an indicator of mortality is 81/672 =0.12, and the NPV is 674/719 = 0.94. Therefore, 12% of patients in the sample whose test results were positive actually died and 94% whose test results were negative survived. The 95% confidence interval for PPV is 10–15% and that for NPV is 92–96%.The prevalence of the disease will alter tha PPV and NPV. When the prevalence is low the PPV will be low, irrespective of the sensitivity and specificity of the test. A higher prevalence will always result in a raised PPV and a lowered NPV [28].

For a sensitivity and specificity of 90 and a d of 10:-

$$\frac{4x90x10}{10^2} = 36$$

We will need at least 36 patients in each cohort who have died 1month after recruitment, and 36 who have lived would be needed. To ensure this we aimed to recruit 200 patients in the palliative care and palliative RT categories

E) Receiver Operating Characteristic Curve (ROC CURVES)

ROC curves were plotted and areas under the curve compared for the different scores. The ROC curve is a graphical technique for assessing the ability of a test to discriminate between those with disease and those without disease. A graph of sensitivity (the true positive rate) against 1 – specificity (the false positive rate) is called a receiver operating characteristic (ROC) curve.A perfect test would have sensitivity and specificity both equal to 1. In order to construct a ROC curve we need to calculate the sensitivity and specicity of the test for each possible cut point value. The ROC curve would start at the origin (0,0),go vertically up the y-axis to (0,1) and then horizontally across to (1,1). A good test would be somewhere close to this ideal. The closer the graph gets to the upper left hand corner (0,1), the better the test is at discriminating between cases and non cases.

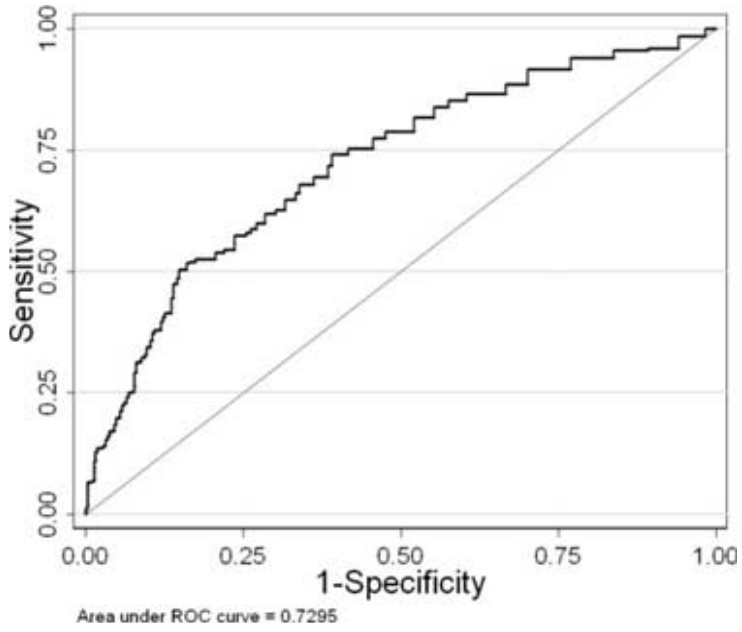
The ROC curve may be used for three purposes:

1. It allows the determination of the cut-off point at which optimal sensitivity and specificity are achieved

2. It allows an assessment of the diagnostic accuracy of a test and

3. It allows the comparison of the usefulness of two or more diagnostic tests.

The performance of a diagnostic variable can be quantified by calculating the area under the ROC curve (AUROC). The ideal test would have an AUROC of 1, whereas a random guess would have an AUROC of 0.5. The performance of a diagnostic variable can be quantified by calculating the area under the ROC curve (AUROC)[30,28,31,32].



F) Median survival

Median survival is defined as The time from either diagnosis or treatment at which half of the patients with a given disease are found to be, or expected to be, still alive [33].

Kaplan Meir curves were plotted to compare the median survivals, with confidence intervals for various classifications: 1) primary diagnosis, 2) secondary diagnosis, 3) Pap and PPI categories, 4) KPS categories, 5) clinician prediction of survival 6) Clinical symptoms 7) laboratory parameters.

G) Confidence interval: The definition of confidence interval is 'a range of values for a variable of interest (the measure of treatment effect) are constructed so that this range has a specified probability of including the true value of the variable. The specified probability is called the confidence level, and the end points of the confidence interval are called the confidence limits'. It is conventional to create confidence intervals at the 95% level – so this means that 95% of the time properly constructed confidence intervals should contain the true value of the variable of interest. The confidence intervals provide a range about the observed effect size. This range is constructed in such a way that we know how likely it is to capture the true – but unknown – effect size [34,35].

The survival analysis provided useful clinical data about the prognosis of patients with advanced cancer, followed up prospectively in India. Unlike in clinical trials, these patients did not have to meet strict inclusion criteria, and are more likely to be representative of patients with incurable cancer in our country.

RESULTS

Table 1a DEMOGRAPHIC DATA

Variables	PALLIATIVE CARE COHORT	
	n	%
Age		
18 – 39	32	16.3
40 – 59	96	48.97
60 – 80	68	34.9
Gender		
Female	123	62.8
Male	73	37.2

Table 1 b

Variables	PALLIATIVE RT COHORT	
	n	%
Age		
18 – 39	20	19.8
40 – 59	61	60.3
60 – 80	20	19.8
Gender		
Female	49	48.5
Male	52	51.5

Table 1c

Variables	COMBINED COHORT	
	n	%
Age		
18 – 39	52	17.5
40 – 59	157	52.9
60 – 80	88	29.6
Gender		
Female	172	57.9
Male	125	42

BASE LINE DIAGNOSTIC CATEGORIES

Table 2a

Primary diagnosis	PALLIATIVE CARE COHORT I
	n
Cervix	39
Head andNeck	21
Lung	10
Breast	14
Colorectal/Oesophagus	15
Ovary	04
Stomach	20
Glioblastoma	02
Gall bladder	05
Not Known	07
Others	22
Secondary diagnosis	
Lung	10
Bone	20
Brain	04
Liver	25
Local recurrence	74
Not known	16
Others	14
Histology	
Squamous cell	60
Adeno	46
Sarcoma	05
Others	32
Not known	23

Table 2b

Primary diagnosis	PALLIATIVE RT COHORT
	n
Cervix	04
Head andNeck	10
Lung	21
Breast	19
Colorectal/Oesophagus	07
Not Known	13
Ovary and others	16
Secondary diagnosis	
Bone	48
Brain	24
Local recurrence	03
Not known	09
Others	09
Histology	
Squamous cell	13
Adeno	40
Sarcoma	01
Others	37
Not known	02

Table 2c

Primary diagnosis	COMBINED COHORT
	n
Cervix	43
Head andNeck	31
Lung	31
Breast	33
Colorectal/Oesophagus	22
Ovary	05
Stomach	20
Glioblastoma	02
Gall bladder	05
Not Known	20
Others	39
Secondary diagnosis	
Lung	10
Bone	68
Brain	28
Liver	25
Local recurrence	77
Not known	25
Others	23
Histology	
Squamous cell	73
Adeno	86
Sarcoma	06
Others	69
Not known	25

Table 3a: PROGNOSTIC CATEGORIES

Variables	PALLIATIVE CARE COHORT
	n
Modified KPS	
More than or equal to 60	132
Between 30 and 50	50
Between 10 and 40	14
Clinician estimated survival	
More than 3 months	79
Between 1 and 3 months	73
Less than or equal to 1month	44

Table 3b:

Variables	PALLIATIVE RADIOTHERAPY COHORT
	n
Modified KPS	
More than or equal to 60	59
Between 30 and 50	35
Between 10 and 40	07
Clinician estimated survival	
More than 3 months	41
Between 1 and 3 months	52
Less than or equal to 1month	08

Table 3c:

Variables	COMBINED COHORT
	n
Modified KPS	
More than or equal to 60	191
Between 30 and 50	85
Between 10 and 40	21
Clinician estimated survival	
More than 3 months	120
Between 1 and 3 months	125
Less than or equal to 1month	52

Table 4a Accuracy of Scores in Predicting One Month Survival :
COHORT 3(COMBINED) – 1 MONTH

	PaP	PPI	MPaP	MPPI	CLINICIAN ESTIMATE SURVIVAL
NUMBER (n)	227	280	282	280	269
Positive Predictive Value PPV	45.5%	67.9%	55.9%	58.5%	59.1%
Negative Predictive Value NPV	82.5%	81.34%	85.2%	82.4%	78.2%
Sensitivity	30.6%	28.8%	50%	36.4%	48.1%
Specificity	89.9%	95.8%	88%	92.1%	91%

Tests of significance

	Value(PaP,MPaP,PPI,MPPI)	Exactsignificance(PaP,MPaP,PPI,MPPI)
Pearson Chi-Square	12.997,44.036,33.869,32.597	0.001,0.000,0.000, 0.000
Likelihood Ratio	11.259,38.962,28.161,27.970	0.001,0.000,0.000, 0.000
Fisher'Exact Test		0.001,0.000,0.000, 0.000

Table 4b Accuracy of Scores in Predicting One Month Survival :
COHORT 1(PAL CARE) -1 MONTH

	PaP	**PPI**	**MPaP**	**MPPI**
NUMBER (n)	132	185	186	185
Positive Predictive Value PPV	60.9%	82.6%	69.76%	71.8%
Negative Predictive Value NPV	77.98%	77.77	82.5%	79.1%
Sensitivity	36.8%	34.5%	54.5%	41.8%
Specificity	90.4%	96.9%	90.1%	93.1%

Tests of significance

	Value(PaP,MPaP,PPI,MPPI)	ExactSignificance(PaP,MPaP,PPI,MPPI)
Pearson Chi-Square	13.984,43.395,35.155,32.898	0.000,0.000,0.000,0.000
Likelihood Ratio	12.758,40.619,32.288,30.216	0.001,0.000,0.000,0.000
Fisher'Exact Test	- -,	0.001,0.000,0.000,0.000

Table 4c Accuracy of Scores in Predicting One Month Survival :
COHORT 2 (PAL RT)-1 MONTH)

	PaP	**PPI**	**MPaP**	**MPPI**
NUMBER (n)	95	90	96	95
Positive Predictive ValuePPV	10%	0	18.8%	11.1%
Negative Predictive Value NPV	82.23	87.8%	90%	88.4%
Sensitivity	9.1%	0	27.3%	9.1%
Specificity	89.3%	94%	84.7%	90.5%

Tests of significance

	Value(PaP,MPaP,PPI,MPPI)	Exactsignificance(PaP,MPaP,PPI,MPPI)
Pearson Chi-Square	0.027,1.006,0.691,0.002	1.000,0.386,0.634,1.000
Likelihood Ratio	0.028,0.895,1.266,0.002	1.000,0.386,0.634,1.000
Fisher'Exact Test		1.000,0.386,1.000,1.000

Table 4d Accuracy of Scores in Predicting Three Month Survival :
COMBINED COHORT-3 MONTHS

	PaP	**PPI**	**MPaP**	**MPPI**	**CLINICIAN ESTIMATE SURVIVAL**
NUMBER (n)	217	269	271	269	259
Positive Predictive Value PPV	67.3%	78.6%	78.7%	78.2%	55.8%
Negative Predictive Value NPV	68.8%	56.6%	61.4%	68.9%	65.7%
Sensitivity	67.9%	39%	52.1%	56%	76.1%
Specificity	68.2%	88.2%	84.4%	82.7%	56%

Tests of significance

	Value(PaP,MPaP,PPI,MPPI)	ExactSignificance(PaP,MPaP,PPI,MPPI)
Pearson Chi-Square	16.954,37.371,24.273,24.300	0.000,0.000,0.000,0.000
Likelihood Ratio	18.137,41.699,30.277,27.307	0.000,0.000,0.000,0.000
Fisher'Exact Test	17.847,40.802,29.001,26.708	0.000,0.000,0.000,0.000

Table 4e Accuracy of Scores in Predicting Three Month Survival : COHORT 1 (PAL CARE)-3 MONTH.

	PaP	**PPI**	**MPaP**	**MPPI**
NUMBER (n)	123	175	176	175
Positive Predictive Value PPV	78.9%	84%	87.3%	81.9%
Negative Predictive Value NPV	59.1%	48%	53.1%	53.4%
Sensitivity	62.5%	39.3%	50.9%	55.1%
Specificity	76.5%	88.2%	88.2%	80.9%

Tests of significance

	Value(PaP,MPaP,PPI,MPPI)	Exact significance(PaP,MPaP,PPI,MPPI)
Pearson Chi-Square	6.754, 19.720, 13.273, 14.327	0.010, 0.000,0.000,0.000
Likelihood Ratio	7.388, 22.905, 17.030, 16.868	0.010,0.000,0.000,0.000
Fisher'Exact Test		0.010,0.000,0.000,0.000

Table 4f Accuracy of Scores in Predicting Three Month Survival : COHORT 2(PAL RT) 3 MONTH.

	PaP	**PPI**	**MPaP**	**MPPI**
NUMBER (n)	94	94	95	94
Positive Predictive Value PPV	54%	65%	61.3%	68.9%
Negative Predictive Value NPV	83.7%	71.2%	76.2%	78.1%
Sensitivity	79.4%	38.2%	55.9%	58.8%
Specificity	61%	88.1%	80%	84.7%

Tests of significance.

	Value(PaP,MPaP,PPI,MPPI)	ExactSignificance(PaP,MPaP,PPI,MPPI)
Pearson Chi-Square	9.323,17.321,9.319,7.476	0.034,0.000,0.058,0.105
Likelihood Ratio	9.141,17.085,10.673,7.295	0.013,0.000,0.006,0.037
Fisher'Exact Test	9.317,16.715,9.810,7.657	0.006,0.000,0.006,0.012

ROC CURVES

COHORT 1 PALLIATIVE CARE . 1 MONTH (Fig 1)

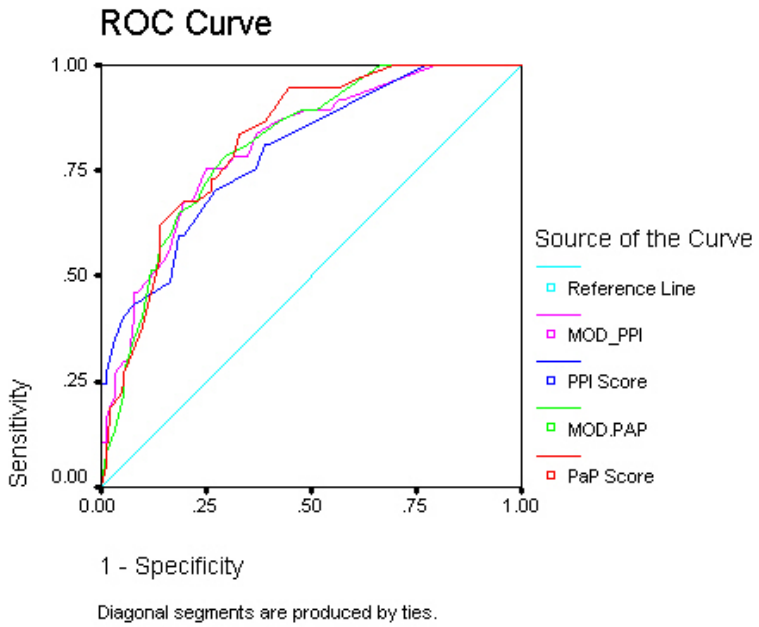


Table 5a: AREA UNDER CURVE (AUC)

Test Result Variable(s)	Area	Std. Error(a)	Asymptotic Sig.(b)	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
PaP Score	.821	.037	.000	.748	.895
MOD.PAP	.811	.039	.000	.734	.887
PPI Score	.794	.043	.000	.711	.878
MOD_PPI	.810	.041	.000	.731	.890

COHORT 2 PALLIATIVE RADIOTHERAPY – 1 MONTH (Fig 2)

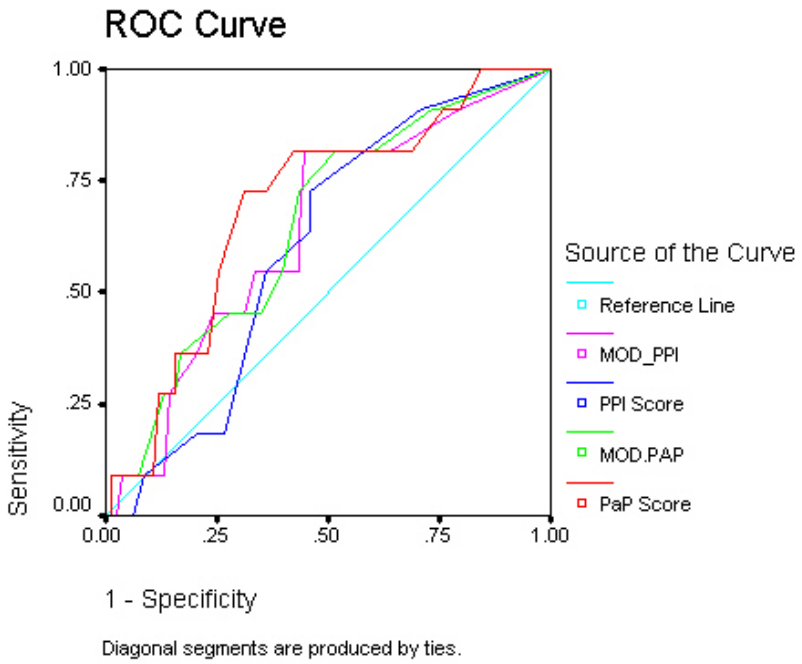


Table 5b: AREA UNDER CURVE (AUC)

Test Result Variable(s)	Area	Std. Error(a)	Asymptotic Sig.(b)	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
PaP Score	.693	.080	.038	.536	.849
MOD.PAP	.652	.083	.102	.489	.815
PPI Score	.604	.076	.266	.455	.752
MOD_PPI	.640	.084	.132	.476	.804

COHORT 3 COMBINED CATEGORY -1 MONTH (Fig 3)

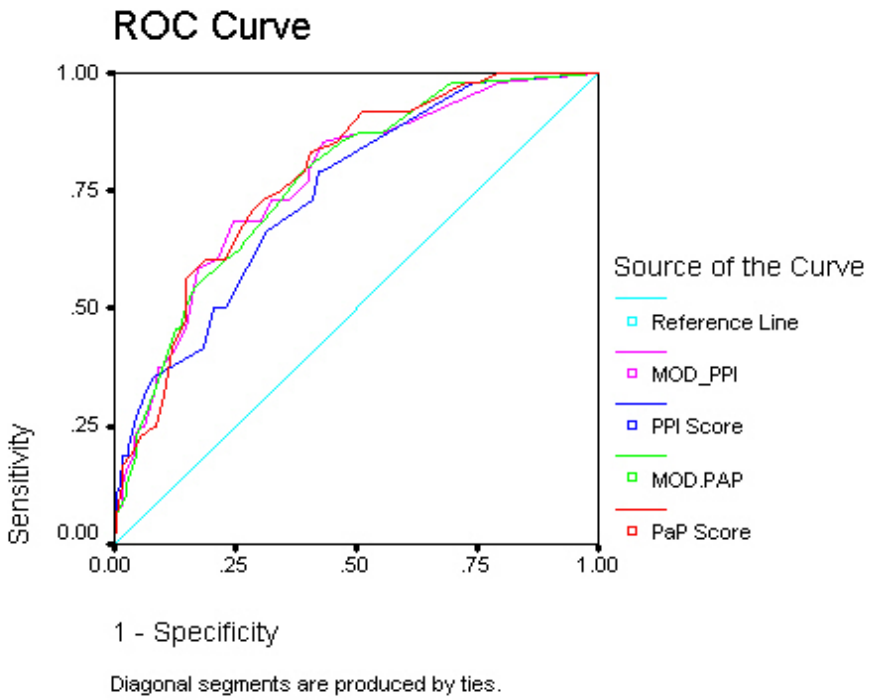


Table 5c: AREA UNDER CURVE (AUC)

Test Result Variable(s)	Area	Std. Error(a)	Asymptotic Sig.(b)	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
PaP Score	.780	.035	.000	.712	.849
MOD.PAP	.771	.036	.000	.700	.842
PPI Score	.744	.038	.000	.669	.819
MOD_PPI	.770	.037	.000	.696	.843

Fig 4 -COHORT 1 PALLIATIVE CARE . 3 MONTH

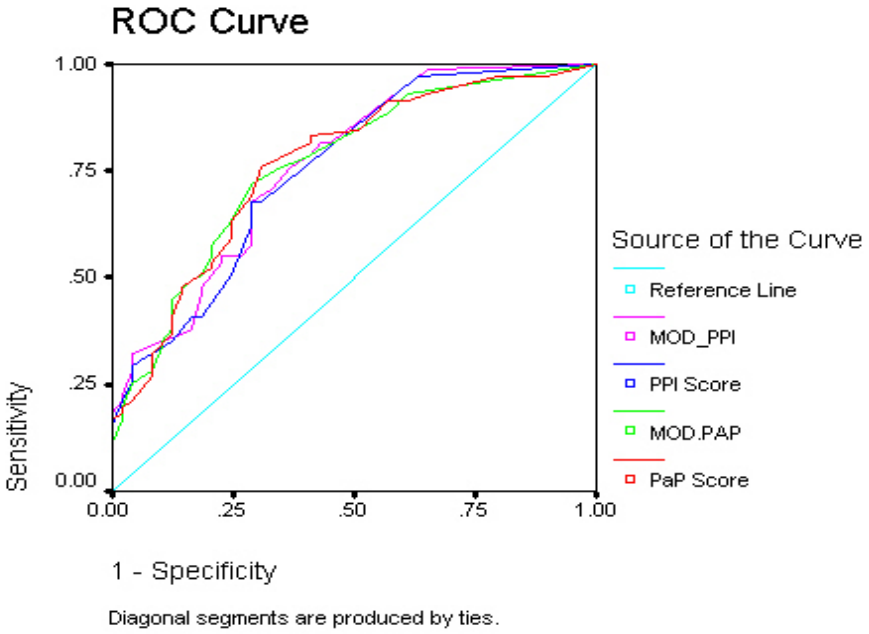


Table 5d: AREA UNDER CURVE (AUC)

Test Result Variable(s)	Area	Std. Error(a)	Asymptotic Sig.(b)	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
PaP Score	.766	.044	.000	.680	.853
MOD.PAP	.765	.044	.000	.679	.851
PPI Score	.755	.045	.000	.667	.843
MOD_PPI	.767	.044	.000	.681	.853

COHORT 2 PALLIATIVE RADIOTHERAPY – 3 MONTH (Fig 5)

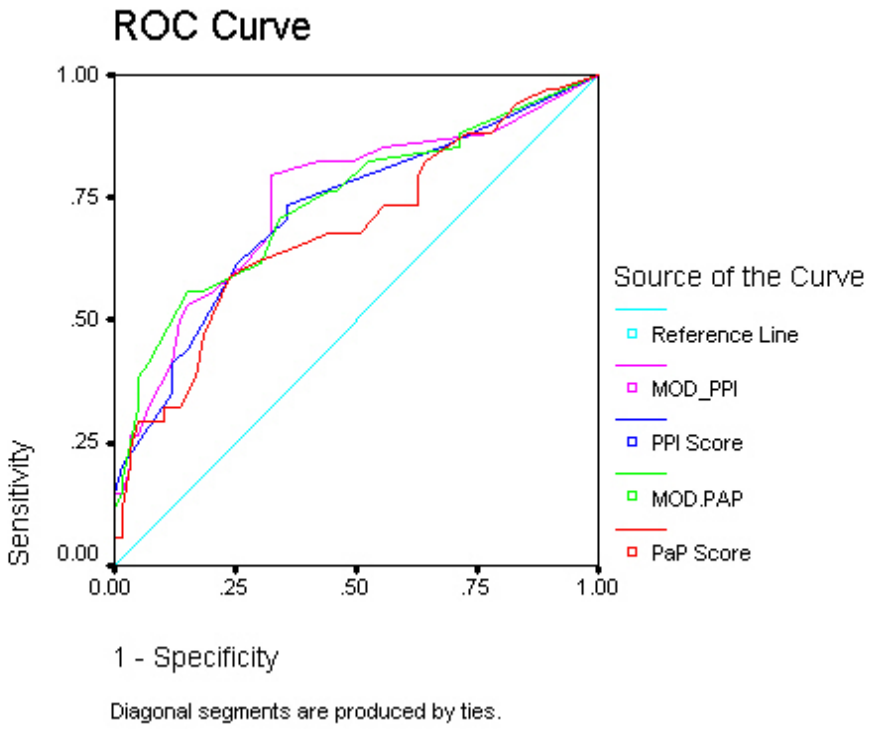


Table 5e: AREA UNDER CURVE (AUC)

Test Result Variable(s)	Area	Std. Error(a)	Asymptotic Sig.(b)	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
PaP Score	.683	.059	.003	.567	.799
MOD.PAP	.739	.056	.000	.629	.849
PPI Score	.721	.057	.000	.609	.833
MOD_PPI	.744	.056	.000	.634	

Fig 6-COHORT 3 COMBINED CATEGORY - 3 MONTH

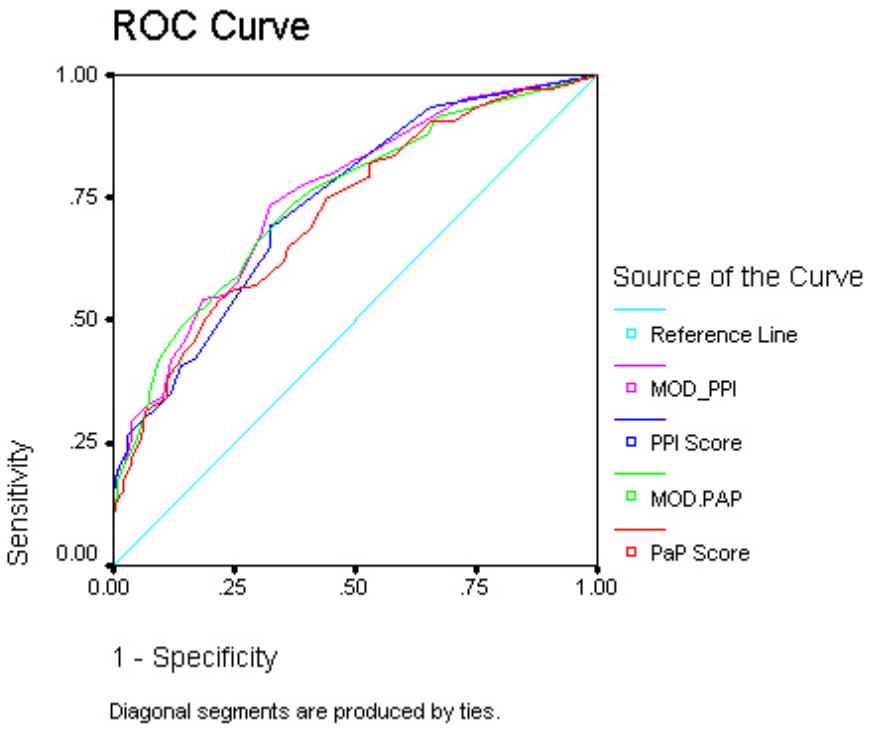


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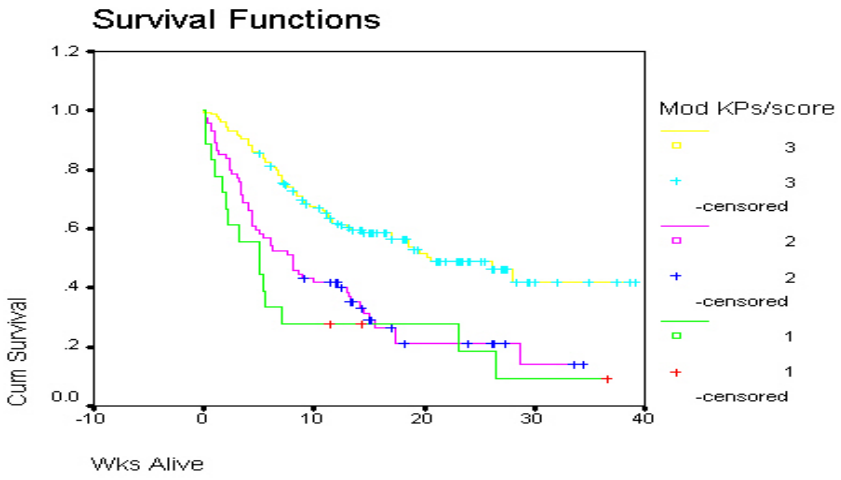
Table 5f : AREA UNDER CURVE (AUC)

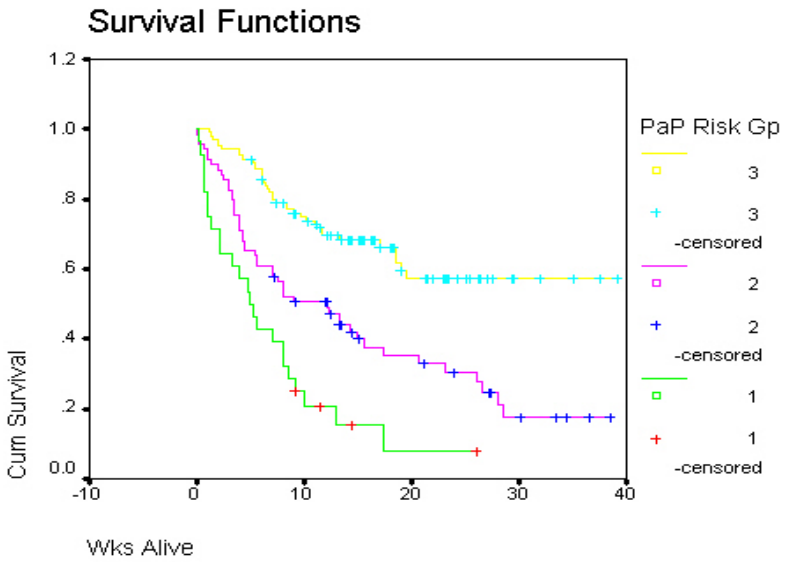
Test Result Variable(s)	Area	Std. Error(a)	Asymptotic Sig.(b)	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
PaP Score	.719	.035	.000	.651	.787
MOD.PAP	.746	.033	.000	.680	.811
PPI Score	.738	.033	.000	.673	.804
MOD_PPI	.756	.033	.000	.692	.820

Fig 7 Survival Curves Based on KPS Category, Combined Cohort



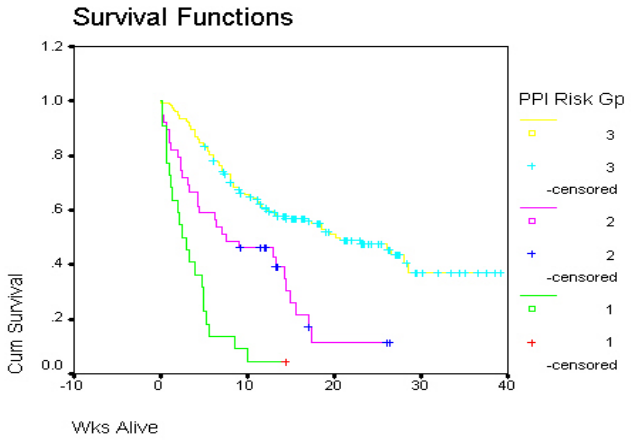
- KPS1: Modified KPS score 10-20.
- KPS2:Modified KPS score 30-50.
- KPS3:Modified KPS score more than 60.

Fig 8 Survival Curves Based on PaP Category, Combined Cohort



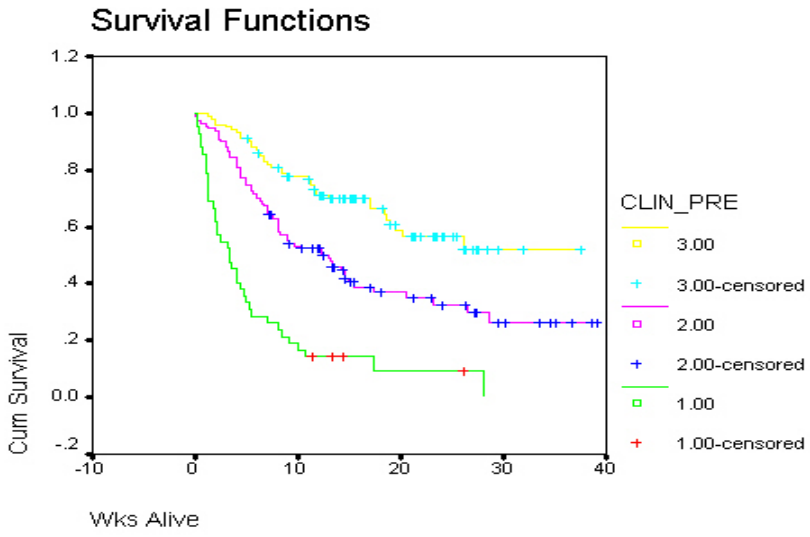
- PaP 1:Risk group C
- PaP 2:Risk group B
- PaP 3:Risk group A

Fig 9 Survival Curves Based on PPI Category, Combined Cohort



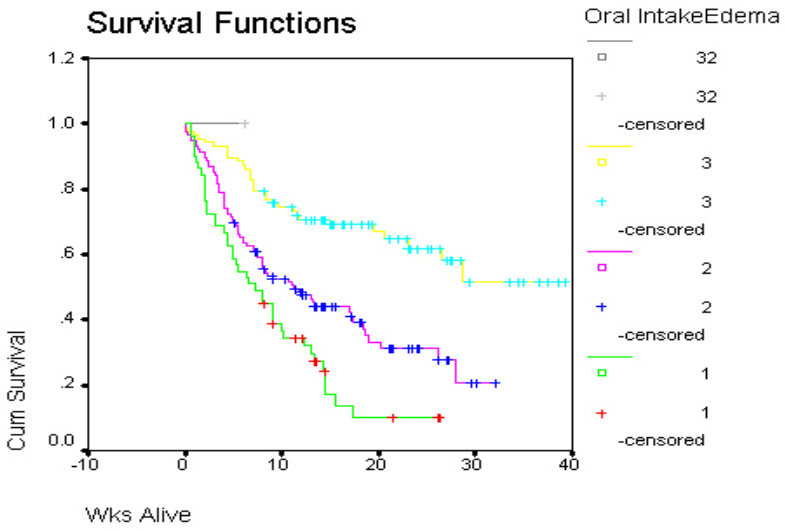
- PPI 1:Risk group C
- PPI 2:Risk group B
- PPI 3:Risk group A

Fig 10 Survival Curves Based on CPS Category, Combined Cohort



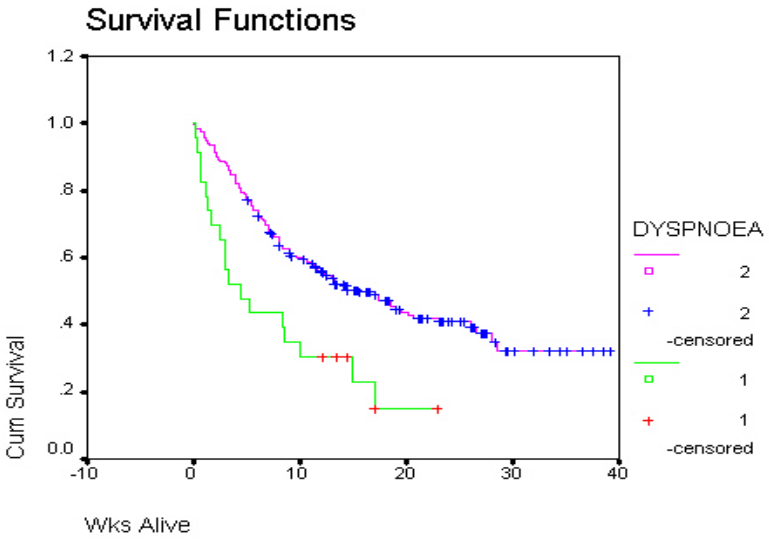
- Clinician Prediction Survival 1:Survival less than or equal 1month.
- Clinician Prediction Survival 2:Survival 1 to 3 months.
- Clinician Prediction Survival 3:Survival more than 3 months.

Fig 11 Survival Curves Based on Oral intake Category, Combined Cohort



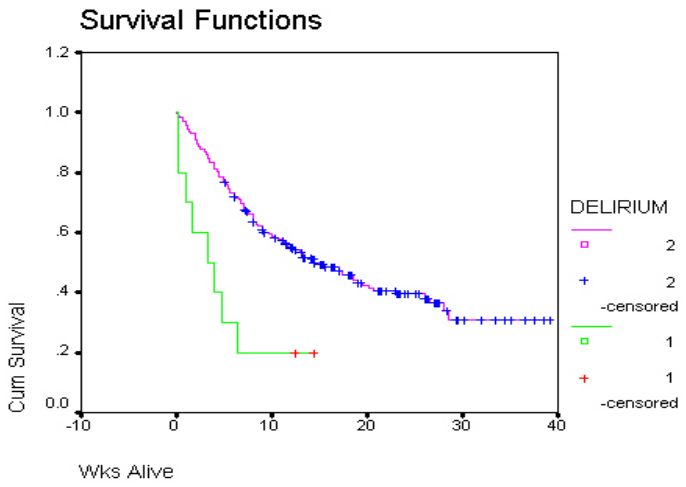
- Oral intake 1: Severely reduced
- Oral intake 2: Moderately reduced.
- Oral intake 3:Normal

Fig 12 Survival Curves Based on Dyspnoea Category, Combined Cohort



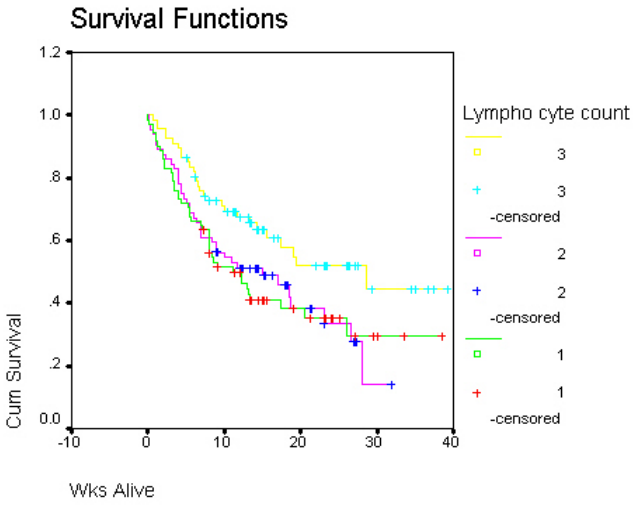
- Dyspnoea 1: Present.
- Dyspnoea 2: Absent.

Fig 13 Survival Curves Based on Delirium Category, Combined Cohort



- Delirium 1: Present.
- Delirium 2: Absent.

Fig 14 Survival Curves Based on Lymphocyte count Category, Combined Cohort



- Lymphocyte 1: Very low(0-11.9%).
- Lymphocyte 2:Low(12-19.9%).
- Lymphocyte 3:Normal(20-40%).

Table 6 a: Median Survival Based On Diagnostic Category In Combined Cohort.

Primary site	Number(n)	Median	Confidence interval	Mean	Confidence interval
Cervix	41	17.1	6.11 , 28.09	16.73	12.83 , 20.64
Head/neck	33	14.50	9.84 , 19.16	19.44	13.75 , 25.13
Lung	31	8	4.18 , 11.82	15.76	10.74, 20.78
Colorectal	12	8.40	0.00 , 19.05	14.14	7.81 , 20.47
Breast	34	17.30	4.5 , 30.10	20.65	15.34, 25.96
Unknown	19	13.30	--	15.27	10.80 , 19.74
Others	41	18.60	13.35,23.85	19.37	14.20, 24.54
Ovary	05	-	-	10.30	5.13 , 15.47
Glioblastoma	02	0.1	-	1.65	0.00, 4.69
Oesophagus	08	-	-	22.53	12.75, 32.31
Gallbladder	05	9.10	1.77, 16.43	8.94	4.73, 13.15
Stomach	21	8.0	2.79, 13.21	11.21	6.69, 15.74

Table 6b: Mean Survival Based On Diagnostic Category In Combined Cohort..

Secondary site	Number(n)	Median	Confidence interval	Mean	Confidence interval
Lung	10	8.50	--	15.44	8.10, 22.78
Bone	67	28	13.90, 42.10	22.96	18.97,26.94
Brain	28	9.00	6.41, 11.59	13.28	9.54, 17.01
Liver	25	8.00	2.45, 13.55	12.71	8.08, 17.33
Local Recurrence	75	11.30	5.25, 17.35	14.48	11.58,17.38
Not known	17	-	-	26.08	18.63, 33.52
Others	22	13.30	3.11, 23.49	15.26	10.68, 19.84

Table 6c: Median Survival Based On Global Assessments.

Category	CLINICIAN ESTIMATE WEEKS(m), (n)	PaP (m),(CI),(n))	PPI (m),(CI),(n)	KPS (m),(CI),(n)
Worst	3.30 (CI 1.58,5.02) N=42	5.0 (CI 3.06,6.94) N=28	2.50 (CI 1.12, 3.88) N=22	5.0 (CI 1.28,8.72). N=18
Intermediate	13.0(CI 8.33,17.67) N=110	12.20(CI 6.73,17.67) N=69	7.50(CI 0.00,15.11) N=39	8.0(CI 5.11,10.89). N=74
Best	Not reached	Not reached	20.20(CI 13.73,26.67) N=189	20.60(CI 14.21,26.99) N=160

- In the clinician estimation categories, confidence intervals did not overlap, indicating better discrimination

Table 6d : Mean Survival Based On Global Assessments

Category	CLINICIAN ESTIMATE WEEKS(m),(CI),(n)	PaP (m),(CI),(n)P	PPI(m),(CI),(n)	KPS(m),(CI),(n)
Worst	6.40 (CI 3.86,8.94) N=42	7.27 (CI 4.42,10.12) N=28	3.67 (CI 2.21,5.13) N=22	10.13 (CI 4.43,15.82) N=18
Intermediate	17.64 (CI 14.60,20.67) N=110	15.54 (CI 12.10,18.98) N=69	10.07 (CI 7.29,12.85) N=39	12.27 (CI 9.36,15.18) N=74
Best	25.28 (CI 22.23,28.34) N=101	26.66 (CI23.43,29.89) N=106	22.10 (CI19.63 ,24.57) N=189	22.93 (CI20.20,25.66) N=160

Table 6e: Median Survival By Symptoms And Lab Tests(W-worst, I-intermediate ,B-best)

	MEDIAN SURVIVAL		CONFIDENCE INTERVAL	MEAN SURVIVAL	CONFIDENCE INTERVAL
ORAL INTAKE	W	7.30 N=51	4.10 , 10.50	9.15	6.92, 11.38
	I	11.20 N=113	6.81, 15.59	14.91	12.56, 17.27
	B	- N=87	--	26.66	23.15, 30.16
DYSPNOEA	W	4.40 N=23	0.80,8.0	8.29	4.92,11.67
	B	15.50 N=229	11.22, 19.78	19.85	17.60, 22.09
DELIRIUM	W	3.20 N=10	0.00,6.76	5.00	1.85,8.15
	B	14.50 N=241	10.20,18.80	19.48	17.29,21.66
LYMPHOCYTE COUNT	W	12.20 N=71	7.05,17.35	17.41	13.53,21.29
	I	15.00 N=64	6.58,23.42	15.59	12.51,18.68
	B	28.60 N=67	13.36,43.84	23.97	19.80,28.13

Discussion

Patients with advanced malignancy are often referred for treatment/supportive care to an oncologist. Decisions regarding the type and duration of treatment need to be based on the possible prognosis, to avoid the errors of unwarranted treatment toxicity or therapeutic nihilism. Estimation of prognosis is also important for families who need to prioritise their personal and social goals.

The accurate prognosis of these patients is often difficult to estimate because of multiple variables such as primary diagnosis, different sites of secondaries, comorbid illness and rapidity of spread. The clinicians use their past experience and medical knowledge to estimate the prognosis, but are not often accurate Hence systematic scoring systems were developed which have been validated in different centres in the world. The use of such scoring systems has been recommeded by the European Association of Palliative Care [2].

In this study we aimed to compare two available prognostic scores the Palliative Prognostic score (PaP) [8] and the Palliative Prognostic Index (PPI) [23] and the Clinician Prediction of survival for predicting one and three month survivals. The PaP score is based on six variables; dyspnoea, anorexia, Karnofsky performance status,clinician prediction of survival,total white blood count,and lymphocyte percentage. The total score ranges from 0 to 17.5 points is separated into three categories:category 3(0-5.5 points) predicts a probability higher than 70% of at least 30 days survival time,category 2 (5.6-11 points) predicts a probability between 30% and 70% ,and finally ,category 1(11.1-17.5 points) predicts a chance lower than 30% of the 1 month survival

time.The PaP was validated for Italian hospice-home care patients in a multicenter study and successfully used for patients with incurable malignancy and end stage non cancer illness. The PPI score does not use lab investigations, but it contains five variables:the performance status(modified Karnofsky scale),oral intake,edema,dyspnoea at rest and delirium . A performance status score lower than 50% predicts a chance of survival of 10% for 6 months [17,27].The sum of score of the PPI ranges from 0 to 15 points.The scores above six points are associated with a 20% survival for 3 weeks ;a sum score above four points are associated with a 20% chance of survival for 6 weeks.The PPI was found to predict 6 week survival with a PPV of 0.91 and a NPV of 0.67.

We also modified the scores MPaP , MPPI after removing the lab investigations from the PaP and adding the Clinician Estimate of Survival to PPI respectively.

Patient population

There were more women than men in the palliative care cohort(Table 1b) .The most common primary diagnosis was cervical malignancy (Table 2a,2c) and it was well correlated with the population based cancer registry datas[36].In females breast cancer is the second most common malignancy in females as per the Madras Metropolitan Tumour Registry[37].

The majority of the patients in the radiotherapy cohort had bone secondaries, (Table 2b) with breast and lung as primary diagnosis. Painful bone metastases are the commonest indication for palliative radiotherapy[38]. The palliative care cohort had a large group of patients with local recurrence of cervical and head and neck cancers.

(Table 2a) as these are common primary cancers in India, and many of these patients were not suitable for further definitive therapy. Stomach cancer was common in the palliative care cohort. This is a common cancer in India [39], but not many patients are suitable for palliative radiotherapy, hence we found fewer patients with stomach cancer in the palliative RT cohort.

Survival scores versus actual survival

One month survival

Combined cohort,one month survival prediction accuracy(Table4a)

All four scores, Pap, PPI, modified Pap and Modified PPI showed highly significant associations ($p < .001$) with the actual one month survival. (Table 4a, Chi square).28(10%)of patients were in PPI category C (code 1) (with a high possibility of death within 1month). Of these 19 died within the month giving a positive predictive value of 67.9%. PPI 's sensitivity was 28.8% because it predicted 19 out of 66 the actual deaths that occurred by one month. Out of the 214 patients who survived one month, 205 were not in category C. The specificity for the test was therefore 95.8%.

Similarly for PAP 33(14.5%) of patients were in PaP category C (code 1) (with a high possibility of death within 1month month). Of these 15 died within the month giving a positive predictive value of 45.5%. PaP 's sensitivity was 30.6% because it predicted 15 out of 49 the actual deaths that occurred by one month. Out of the 178 patients who survived one month, 160 were not in category C. The specificity for the test was therefore 89.9%.

The results of PPI are similar to those reported in the literature.The 6 weeks survival was predicted with a PPV of 83% and NPV of 71% in the study by Morita[23]. A survival of less than 6 weeks was predicted with PPV of 91% and NPV of 64% in the study by Stone etal[21]. Stiel et al reported a specificity of 94% and sensitivity of 51% for three week survival . In the PaP in the category C with less than 30% chance for 30 days survival the sensitivity was 67% and specificity was 100%[27].

Inference

PPI had the highest specificity and PPV of all the four scores, but a low sensitivity. (The best sensitivity 48.1% was in fact was for the clinician's prediction of survival.). The clinician estimated survival category had sensitivity of 48.1%, specificity of 91%,PPV of 59.1% and NPV of 78.2%. PPI is useful in identifying sick patients since it is simple, It can be done easily in the home and hospice settings, and can be quickly scored even by relatively new clinicians. PPI does not use any lab investigations. It is worth noting that removing the laboratory tests did not reduce the predictive accuracy of PaP score at one month. But PPI has limitations it misses some sick patients as evidenced by its low sensitivity. Clinical predictions for individual patients can probably improve this as suggested by Stiel et al [27].

Palliative Care Cohort(Cohort 1)

One month survival prediction accuracy (Table 4b)

All four scores, Pap, PPI, modified Pap and Modified PPI showed highly significant associations ($p < .001$) with the actual one month survival. (Table 4b, Chi

square).23(12.4%) of patients were in PPI category C (code 1) (with a high possibility of death within 1month month). Of these 19 died within the month giving a positive predictive value of 82.6%. PPI 's sensitivity was 34.5% because it predicted 19 out of the 55 actual deaths that occurred by one month. Out of the 130 patients who survived one month, 126 were not in category C. The specificity for the test was therefore 96.9%.

Similarly for PAP 23(17.4%) of patients were in PaP category C (code 1) (with a high possibility of death within 1month. Of these 14 died within the month giving a positive predictive value of 60.9%. PaP 's sensitivity was 36.8% because it predicted 14 out of the 38 actual deaths that occurred by one month. Out of the 94 patients who survived one month, 85 were not in category C. The specificity for the test was therefore 90.4%.

Palliative Radiotherapy Cohort-Cohort 2

One month survival prediction accuracy (Table 4c)

All four scores, Pap, PPI, modified Pap and Modified PPI showed highly significant associations ($p < .001$) with the actual one month survival. (Table 4c, Chi square).5(5.2%) of patients were in PPI category C (code 1) (with a high possibility of death within 1month month).

Out of the total 15(both PaP and PPI) patients, only 1 had expired at one month, hence meaningful statistical analysis or conclusions were not possible. When clinicians expect a short survival of less than one month, patients may not be referred for palliative RT. Among the category C patients who were in this group, many fell into

category C because they had a poor KPS as they were immobile due to bone secondaries, and not because they were critically ill.

3 months survival

Combined cohort, three month survival prediction accuracy (Table 4d)

All four scores, Pap, PPI, modified Pap and Modified PPI showed highly significant associations ($p < .001$) with the actual three month survival. (Table 4d, Chi square).There was 70(26%) of patients were in PPI category B or C (code 1) (with a high possibility of death within 3 month). Of these 55 died within three months giving a positive predictive value of 78.6%. PPI 's sensitivity was 39% because it predicted 55 out of 141 the actual deaths that occurred by three months. Out of the 127 patients who survived three months, 112 were not in category C. The specificity for the test was therefore 88.2%.

Similarly for PAP (107)49.3% of patients were in PaP category B or C (code 1) (with a high possibility of death within 3 month). Of these 72 died within three month giving a positive predictive value of 67.3%. PaP 's sensitivity was 67.9% because it predicted 72 out of the 106 actual deaths that occurred by 3 month. Out of the 110 patients who survived three month, 75 were not in category C. The specificity for the test was therefore 68.2%. These results were similar to the results seen in the literature.

In the PPI the sensitivity for the those with a 20% chance of 6 weeks survival was 46% and specificity was 84% and those with more than 20% chance of 6 week survival had a sensitivity of 83% and specificity of 66%[27].

Palliative care cohort(Cohort 1) Table 4e.

All four scores, Pap, PPI, modified Pap and Modified PPI showed highly significant associations (p< .001) with the actual three month survival. (Table 4e) 50(28.5%) of patients were in PPI category B or C (code 1) (with a high possibility of death within 3 month). Of these 42 died within the month giving a positive predictive value of 84%. PPI 's sensitivity was 39.3% because it predicted 42 out of 107 the actual deaths that occurred by three month. Out of the 68 patients who survived three month, 60 were not in category C. The specificity for the test was therefore 88.2%.

Similarly for PAP 57(46.3%) of patients were in PaP category B or C (code 1) (with a high possibility of death within 3 month). Of these 45 died within the month giving a positive predictive value of 78.9%. PaP 's sensitivity was 62.5% because it predicted 45 out of the 72 actual deaths that occurred by three month. Out of the 51 patients who survived three month, 39 were not in category C. The specificity for the test was therefore 76.5%.

In the Palliative radiotherapy cohort (Table 4f)

All four scores, Pap, PPI, modified Pap and Modified PPI showed highly significant associations (p < .001) with the actual three month survival. (Table 4f, Chi square).20(21.2 %) of patients were in PPI category B or C (code 1) (with a high possibility of death within 3 month). Of these 13 died within the 3 month giving a positive predictive value of 65%. PPI 's sensitivity was 38.2% because it predicted 13 out of the 34 actual deaths that occurred by three month. Out of the 59 patients who

survived three month, 52 were not in category C. The specificity for the test was therefore 88.1%.

Similarly for PaP 50(53.2%) of patients were in PaP category B or C (code 1) (with a high possibility of death within 3 month). Of these 27 died within the three month giving a positive predictive value of 54%. PaP 's sensitivity was 79.4% because it predicted 27 out of the 34 actual deaths that occurred by three month. Out of the 59 patients who survived three month, 36 were not in category C. The specificity for the test was therefore 61%.

Inference

Most reports from literature have not studied the accuracy of these scores in predicting three month survival. In our study PPI had a good PPV and specificity- patients with a poor PPI score were very likely to die in three months. But its sensitivity was very low- it identified less than half of those who died. Estimating three month deaths is more difficult than one month deaths. It is possible that adding clinicians estimates and laboratory tests, may increase accuracy as compared to only symptoms and KPS recorded in PPI. This is reflected in the 76% sensitivity in clinician's estimates, and the two thirds accuracy of Pap in terms of PPV, sensitivity, specifity and NPV. Removing the laboratory tests from PaP reduced its sensitivity for three month survival from 67.9% to 52.1%. Decisions regarding three month survivals are usually needed for determining whether to give longer courses of treatment. In such situations it should be feasible to do lab tests, and get the clinical assessment of an experienced clinician.

ROC curves (Figures 1-6)

ROC curves were generated for all the four scores in the 1 month and more than 3 month survival categories in all the cohorts. (Figures 1-6). There were insufficient events in the palliative RT cohort at one month to draw inferences.

In all other cases, the areas under curve (AUC) (Tables 5a-5f) for all these scores were good, and highly statistically significant.

The AUC for the combined cohorts PaP was 0.780 with CI 0.712 to 0.849, and for PPI 0.744 with CI 0.669 to 0.819 at one month. Removal of laboratory tests did not significantly reduce the AUC (modified Pap AUC) at one month .

The AUC for the combined cohorts PaP was 0.719 with CI 0.651 to 0.787, and for PPI 0.738 with CI 0.673 to 0.804 at three month. .

As there was overlap of the confidence intervals for these scores, no score was clearly superior to the above based on ROC analysis, and the choice of score can be based on convenience, and clinical relevance as discussed in the section on sensitivity and positive predictive value.

Median survivals

A. By primary diagnosis (Table 6a)

In the primary diagnostic category patients with carcinoma cervix, head and neck breast had higher median survivals of 17.1,14.5 and 17.3 weeks respectively. In the literature the median survival for metastatic carcinoma cervix was 4-9 months with

chemotherapy, relapse in nodal region had a 24 weeks survival and relapse in other regions had a median survival of 12 weeks.[40].

Shorter survivals were seen in patients with lung cancer (8 weeks,) colorectal (8.4 weeks),stomach cancer (8 weeks) and carcinoma of the gall bladder(9.1 weeks). As per the cancer statistics from National cancer institute the 5 year relative survival for metastatic lung cancer was only 2% [41].

B. By metastatic site (Table 6b)

Patients with bone metastases had the longest median survivals of 28 wks(CI 13.9 to 42.10).In the RTOG trial the median survival in patients with solitary and multiple bone metastasis was 36 and 24 weeks respectively [42]. Patients with brain metastases had a median survival of 9 weeks in good comparison with the literature; patients in RPA class 3(KPS less than 70 ,age more than 65 years and uncontrolled primary tumour have median survival of 2 months[43].Patients with local recurrence had longer survivals than brain metastases but shorter than bone metastases (11.3 weeks, CI 5.25 to 17.35).

C. Median survival by symptoms (Table 6e and figures 11 to 14)

The median survival based on the patients symptoms showed that patients who had dyspnoea and delirium had lowest median survival 4.4 weeks (confidence intervals 0.8 to 8) and 3.2 weeks (confidence intervals 0.00 to 6.76).In other symptom categories there was considerable overlap in the confidence intervals and hence they are not as

reliable as dyspnoea and delirium. In the study by Morita et al the performance status 10-20 with dyspnoea at rest and presence of delirium was associated with a survival of less than 3 week. In the multiple regression analysis the regression coefficients ± standard error for Dyspnea at rest 0.88±0.16 and partial score was 3.5 and for Delirium it was 1.0 ±0.17, 4.0 respectively[23].In the study by Pirovano et al dyspnoea was independent variable with prognostic Value[8]

D Median survival by global assessments

D.1 Clinician Estimate of Survival (Table 6c,6d ,Figures 7-10)

The Pap score needs the clinician to classify survival in two week increments upto three months. Based on this prospective assessment we were able to catrtegorize patients into worst prognosis (clinician estimate less than four weeks), intermediate prognosis (I month to less than three months) and better prognosis (more than 3 months).

In the Clinician estimate survival for the combined category, those estimated to live less than four weeks had an actual median survival of 3.3 weeks with a 95% confidence interval between 1.58 and 5.02 . Those estimated to live between one to three months (intermediate group) had a median survival of 13 weeks with a 95% confidence interval between 8.33 and 17.67.There was no overlap of the confidence interval and hence it was good tool discriminating these groups.In the good prognostic categories the median survival was not yet reached as more than 50% of patien ts were

still alive, but it was greater than 20 weeks. Further follow up is necessary to document the median survival.

D.2 PPI

In the combined category, those estimated to live less than four weeks had an actual median survival of 2.5 weeks with a 95% confidence interval between 1.12 and 3.88. Those estimated to live between one to three months (intermediate group) had a median survival of 7.50 weeks with a 95% confidence interval between 0.00 and 15.11. In the good prognostic categories the median survival was 20.20 weeks with a 95% confidence interval between 13.73 to 26.67.

D.3 PAP

In the combined category, those estimated to live less than four weeks had an actual median survival of 5 weeks with a 95% confidence interval between 3.06 and 6.94. Those estimated to live between one to three months (intermediate group) had a median survival of 12.2 weeks with a 95% confidence interval between 6.73 and 17.67.

KPS

In the combined category, those estimated to live less than four weeks had an actual median survival of 5 weeks with a 95% confidence interval between 1.28 and 8. 72 . Those estimated to live between one to three months (intermediate group) had a median survival of 8 weeks with a 95% confidence interval between 5.11 and 10.89. In the good prognostic categories the median survival was 20.60 weeks with a 95% confidence interval between 14.21 to 26.99.

CONCLUSION

1) All scores were highly statistically significant prediction of the survivals in the population studied. These tests were less specific for individual patients, except those who are very sick.

2) Clinician estimate was as good as other scores for less than 1 month and more 3 month categories. It had a better sensitivity compared to the PPI score. Hence even with availability of these scores its value should not be negligible.

3) No score was superior to another as seen in the ROC curves.

   There was no loss of AUC by removing laboratory investigations from the Pap Score for predicting on month survival

4) PPI was a simple score and useful especially in very sick patients, to predict one month survival.

5) Three month survival prediction is possibly more accurate by incorporating lab tests and clinician estimates than by PPI scores alone.

The shortest median survivals were for PPI category C. The longest were for patients where the clinician estimated more than three months.

6) Bone secondaries had the longest survival by metastatic site and many patients could be considered for further systemic therapy to improve survival, especially if they have good Pap or PPI scores.

7) Patients with local recurrence had survivals in the range, median survival 11.3 weeks with confidence intervals from 5.25 to 17.35. Many of these patients are not suitable for further radiotherapy, and it is necessary to improve the quality of life (QOL) through good palliative care.

8) Patients with brain metastases, lung cancer and stomach cancer have shorter survivals, and decisions regarding long or expensive courses of treatment should be made judiciously.

BIBLIOGRAPHY

1. Glare P, Virik K.Independent prospective validation of the PaP score in terminally ill patients referred to a hospital-based palliative medicine consultation service. J Pain Symptom Manage (2001) 22:891–898 .

2. Maltoni M, Caraceni A,. Brunelli C, Broeckaert B, Christakis N,Eychmuelle S et al Prognostic Factors in Advanced Cancer Patients:Evidence-Based Clinical Recommendations A Study by the Steering Committee of the European Association for Palliative Care J Clin Oncol 23:6240-6248.

3. Lamont EB, Christakis NA. Prognostic disclosure to patients with cancer near the end of life. Ann Intern Med (2001) 134:1096-1105.

4. Christakis NA, Lamont EB. Extent and determinants of error in doctors' prognoses in terminally ill patients: prospective cohort study. B M J. 2000;320:469–473

5. Oxenham D, Cornbleet MA. Accuracy of prediction of survival by different professional groups in a hospice. Palliat Med 1998; 12: 117–18.

6. Glare P, Virik K, Jones M, Hudson M, Eychmuller S, Simes J et al. A systematic review of physicians' survival predictions in terminally ill cancer patients. BMJ 2003Jul 26;327(7408):195-198.

7. Vigano` A, Dorgan M, Buckinham J, Bruera E, Suarez-Almazor ME.Survival prediction in terminal cancer patients: a systematic review of the medical literature. Palliat Med 2000 sept;14(5):363– 74.

8. Pirovano M, Maltoni M, Nanni O, Marinari M, Indelli M, Zaninetta G et al. A new Palliative Prognostic Score: a first step for the staging of terminally ill cancer patients. J Pain Symptom Management 1999; 17: 231–39.

9. Bruera E, Miller MJ, Kurhn N, MacEachern T,Hanson J.Estimate of survival of patients admittedto a palliative care unit: a prospective study. J Pain Symptom Manage 1992; 7: 82–86.

10. Maltoni M, Nanni O, Derni S , Innocenti M. P, Fabbri L, Riva N. et al.Clinical prediction of survival is more accurate than the Karnofsky Performance Status in estimating lifespan of terminally ill cancer patients. Eur J Cancer 1994; 30A: 764–66.

11. Maltoni M, Pirovano M, Scarpi E, Mauro Marinari, Monica Indelli, Ermenegildo Arnoldi. et al. Prediction of survival of patients terminally ill with cancer. Results of an Italian Prospective Multicentric Study.Cancer 1995;75(10):2613 –22.

12. Vigano` A, Bruera E, Jhangri ,GS Newman SC, Fields AL, Suarez-Almazor ME. Clinical survival predictors in patients with advanced cancer. Arch Intern Med. 2000 Mar 27;160 (6):861-8.

13. Vigano A, Dorgan M, Bruera E, Suarez-Almazor ME.The relative accuracy of the clinical estimation of the duration of life for patients with end of lifecancer. Cancer 1999; 86: 170–76.

14. M. Maltoni, D. Amadori . Hematol Oncol Clin N Am 16 (2002) 715–729.

15. Lamont EB, Christakis NA. Some elements of prognosis in terminal cancer. Oncology 1999;13(8):1165–70.

16. Evans C, McCarthy M.Prognostic uncertainty in terminal care: can the Karnofsky Index help? Lancet 1985; 25: 1204–06.

17. Anderson F, Downing GM, Hill J, Casorso L, Lerch N.Palliative performance Scale (PPS): a new tool. J Palliat Care1996;12(1): 5–11.

18. Bachelot T, Ray-Coquard I, Catimel G, C. Ardiet, J. P. Guastalla, A. Dumortier et al. Multivariate analysis of prognostic factors for toxicity and survival for patients enrolled in phase I clinical trials. Ann Oncol 2000;11(2): 151– 6.

19. Janisch L, Mick R, Schilsky RL, Vogelzang NJ, O'Brien S, Kut M, Ratain MJ. Prognostic factors for survival in patients treated in phase I clinical trials. Cancer 94;74(7):1965– 73.

20. Paul A. Glare, Steffen Eychmueller , Patrick McMahon.Diagnostic Accuracy of the Palliative Prognostic Score in Hospitalized Patients With Advanced Cancer. Journal of Clinical Oncology, Vol 22, No 23

21. Maltoni M, Nanni O, Pirovano M , Scarpi E, Indelli M, Martini C, et al. Successful validation of the Palliative Prognostic Score in interminally ill cancer patients. J Pain Symptom Management 1999; 17: 240–47.

22. Davide Tassinari, Luigi Montanari , Marco Maltoni ,Michela Ballardini , Alessandra Piancastelli ,Marco Musi et al .Support Care Cancer (2008) 16:359–370

23. Morita T, Tsunoda J, Inoue S, Chihara S.The Palliative Prognostic Index: a scoring system for survival prediction of terminally ill cancer patients.Support Care Cancer 1999; 7: 128–33. December 1), 2004: pp. 4823-4828

24. Morita T, Tsunoda J, Inoue S, Chihara S. Improved accuracy of physicians' survival prediction for terminally ill cancer patients using the Palliative Prognostic Index. Palliat Med 2001; 15: 419–424.

25. P.C.Stone, S.Lund.Predicting prognosis in patients with advanced cancer.Annals of Oncology 18: 971–976, 2007

26. Stone CA, Tiernan E , and Dooley BA .Prospective Validation of the Palliative Prognostic Index in Patients with Cancer.J Pain Symptom Management 2008;35:617—622.

27. S. Stiel , L. Bertram , S. Neuhaus, F. Nauck,C. Ostgathe , F. Elsner & L. Radbruch , Evaluation and Comparison of Prognostic scores and the Physician estimate of Survival in Terminally ill Patients. Support Care Cancer (2010) 18:43–49

28. Statistics review 13: Receiver operating characteristic curves,Viv Bewick, Liz Cheek and Jonathan Ball ,Critical Care December 2004 Vol 8 No 6 Review.

29. Parks Text book of preventive and social medicine, 2002.

30. Understanding diagnostic tests 3: receiver operating characteristic curves Anthony K Akobeng ,Acta Pædiatrica 2007 96, pp. 644–647

31. Altman DG, Bland JM. Diagnostic tests 3: receiver operating characteristic plots. BMJ 1994; 309: 188.

32. O'Connell B and Myers H. Journal of Clinical Nursing, 11, 134±136.

33. www.cancer.gov/dictionary/ accessed on Dec 2009.

34. Last JM. A Dictionary of Epidemiology. Oxford:International Journal of Epidemiology, 1988,

35. Huw TO Davies ,Iain K Crombie, University of Dundee, www.whatisseries.co.ukAcessed in Dec 2009

36. Nandakumar A, Ramnath T & Chaturvedi M. The magnitude of cancer cervix in India .Indian J Med Res 130, September 2009, pp 219-221.

37. C. K. Gajalakshmi, V. Shanta, R. Swaminathan, R. Sankaranarayanan, and R. J. Black A population-based survival study on female breast cancer in Madras, India Br J Cancer. 1997; 75(5): 771–775

38. Nielsen OS, Munro AJ and Tannock IF , Bone metastases: pathophysiology and management policy .Journal of Clinical Oncology, Vol 9, 509-524

39. Pavithran K, Dinesh C D, and Kamal K, Gastric cancer in India P.Gastric Cancer (2002) 5: 240–243.

40. Michael F, Michelle G. Guidelines for the Treatment of Recurrent and Metastatic Cervical Cancer . The Oncologist, Vol. 7, No. 4, 342–347, August 2002

41. Ries L, Eisner M, Kosary C: Cancer Statistics Review, 1975-2002. Bethesda, Md: National Cancer Institute, 2005 http://seer.cancer.gov/csr/1975_2002.

42. Tong D, Gillick L, Hendrickson F R .The palliation of symptomatic osseous metastases final results of the study by the radiation therapy oncology group (p 893-899).Cancer. Volume 50 Issue 5 ,

43. Gaspar L,Scott C,Rotman M,Asbell S, Phillips T, Wasserman T et al Recursive partitioning analysis (RPA) of prognostic factors in three radiation therapy oncology group (RTOG) brain metastases trials.International Journal of Radiation Oncology * Biology * Physics. Volume 37, Issue 4, Pages 745-751

APPENDIX I

ROC Curve Cordinates

Coordinates of the Curve			
Test Result Variable(s)	Positive if Greater Than or Equal To(a)	Sensitivity	1 - Specificity
PaP Score	-1.00	1.000	1.000
	.25	1.000	.928
	.75	1.000	.916
	1.25	1.000	.843
	1.75	.909	.795
	2.25	.909	.759
	2.75	.818	.687
	3.25	.818	.663
	3.75	.818	.639
	4.25	.818	.590
	4.75	.818	.530
	5.25	.818	.494
	5.75	.818	.482
	6.25	.818	.422
	6.75	.727	.361
	7.25	.727	.313
	7.75	.545	.253
	8.25	.364	.229
	8.75	.364	.205
	9.25	.364	.181
	9.75	.364	.157
	10.25	.273	.157
	10.75	.273	.120
	11.50	.091	.108
	12.25	.091	.096
	12.75	.091	.048

	13.25	.091	.036
	13.75	.091	.024
	14.25	.091	.012
	14.75	.000	.012
	16.00	.000	.000
MOD.PAP	-1.000	1.000	1.000
	.500	.909	.747
	1.250	.909	.735
	1.750	.818	.602
	2.250	.818	.530
	3.000	.818	.518
	3.750	.727	.434
	4.250	.545	.398
	4.750	.455	.349
	5.250	.455	.301
	5.750	.455	.289
	6.250	.455	.277
	6.750	.364	.169
	7.250	.273	.157
	7.750	.273	.145
	8.250	.273	.133
	9.000	.091	.072
	9.750	.091	.060
	10.500	.091	.036
	11.500	.091	.012
	12.250	.000	.012
	13.500	.000	.000
PPI Score	-1.00	1.000	1.000
	.50	.909	.711
	1.50	.727	.458
	2.25	.636	.458
	3.00	.545	.361

	3.75	.182	.265
	4.25	.182	.229
	4.75	.182	.205
	5.50	.091	.084
	6.25	.000	.060
	7.00	.000	.048
	7.75	.000	.036
	8.25	.000	.024
	9.75	.000	.012
	12.00	.000	.000
MOD_PPI	-1.00	1.000	1.000
	.50	.909	.795
	1.50	.818	.639
	2.25	.818	.578
	2.75	.818	.530
	3.25	.818	.446
	3.75	.636	.434
	4.25	.545	.434
	4.75	.545	.373
	5.25	.545	.337
	5.75	.455	.313
	6.25	.455	.265
	6.75	.455	.241
	7.25	.364	.205
	7.75	.273	.145
	8.25	.091	.133
	9.00	.091	.120
	10.00	.091	.108
	10.75	.091	.096
	11.50	.091	.060
	13.00	.091	.048
	14.25	.091	.036

	15.25	.000	.024
	16.50	.000	.012
	18.00	.000	.000
The test result variable(s): PaP Score, MOD.PAP, PPI Score, MOD_PPI has at least one tie between the positive actual state group and the negative actual state group.			
a The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.			

ROC Curve

Coordinates of the Curve			
Test Result Variable(s)	Positive if Greater Than or Equal To(a)	Sensitivity	1 – Specificity
PaP Score	-1.00	1.000	1.000
	.25	1.000	.920
	.75	1.000	.886
	1.25	1.000	.794
	1.75	.979	.754
	2.25	.979	.726
	2.75	.938	.651
	3.25	.917	.611
	3.75	.917	.589
	4.25	.917	.514
	4.75	.854	.457
	5.25	.833	.406
	5.75	.792	.394
	6.25	.750	.343
	6.75	.729	.309
	7.25	.708	.286
	7.75	.667	.257

	8.25	.604	.229
	8.75	.604	.206
	9.25	.604	.189
	9.75	.563	.149
	10.25	.479	.149
	10.75	.417	.120
	11.25	.313	.103
	11.75	.250	.086
	12.25	.250	.080
	12.75	.229	.051
	13.25	.208	.046
	13.75	.188	.034
	14.25	.167	.017
	14.75	.125	.017
	15.25	.063	.006
	16.50	.042	.006
	18.50	.000	.000
MOD.PAP	-1.000	1.000	1.000
	.500	.979	.737
	1.250	.979	.697
	1.750	.875	.554
	2.250	.875	.503
	3.000	.854	.469
	3.750	.792	.389
	4.250	.729	.343
	4.750	.688	.309
	5.250	.646	.269
	5.750	.625	.257
	6.250	.604	.229
	6.750	.542	.166
	7.250	.500	.149
	7.750	.458	.137

	8.250	.458	.126
	9.000	.333	.086
	9.750	.292	.069
	10.250	.229	.046
	10.750	.188	.046
	11.500	.125	.023
	12.250	.104	.023
	13.000	.063	.006
	14.500	.000	.000
PPI Score	-1.00	1.000	1.000
	.50	.979	.743
	1.25	.792	.429
	1.75	.792	.423
	2.25	.729	.411
	3.00	.667	.314
	3.75	.500	.229
	4.25	.500	.206
	4.75	.417	.183
	5.25	.354	.080
	5.75	.333	.069
	6.25	.271	.046
	6.75	.208	.029
	7.25	.188	.029
	7.75	.188	.017
	8.25	.125	.011
	8.75	.104	.006
	9.75	.083	.006
	10.75	.063	.006
	11.25	.063	.000
	11.75	.042	.000
	13.50	.021	.000
	16.00	.000	.000

MOD_PPI	-1.00	1.000	1.000
	.50	.979	.794
	1.25	.896	.606
	1.75	.896	.600
	2.25	.875	.560
	2.75	.875	.509
	3.25	.854	.429
	3.75	.792	.400
	4.25	.771	.400
	4.75	.729	.360
	5.25	.729	.326
	5.75	.688	.303
	6.25	.688	.263
	6.75	.688	.246
	7.25	.604	.211
	7.75	.583	.171
	8.25	.458	.149
	8.75	.438	.137
	9.25	.417	.126
	9.75	.375	.097
	10.25	.375	.091
	10.75	.333	.086
	11.50	.250	.063
	12.25	.250	.051
	12.75	.229	.040
	13.25	.208	.040
	13.75	.188	.040
	14.25	.167	.029
	14.75	.125	.017
	15.05	.104	.017
	15.55	.083	.017
	16.50	.083	.006

	17.50	.083	.000
	18.25	.063	.000
	19.25	.042	.000
	21.75	.021	.000
	24.50	.000	.000

The test result variable(s): PaP Score, MOD.PAP, PPI Score, MOD_PPI has at least one tie between the positive actual state group and the negative actual state group.

a The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

ROC Curve

Coordinates of the Curve			
Test Result Variable(s)	Positive if Greater Than or Equal To(a)	Sensitivity	1 - Specificity
PaP Score	-1.00	1.000	1.000
	.25	.972	.898
	.75	.972	.796
	1.25	.930	.653
	1.75	.915	.612
	2.25	.915	.571
	2.75	.845	.510
	3.25	.831	.408
	3.75	.817	.408
	4.25	.761	.306
	4.75	.690	.286
	5.25	.634	.245
	5.75	.592	.245
	6.50	.535	.204
	7.50	.521	.204
	8.25	.493	.163

	8.75	.479	.143
	9.25	.465	.143
	9.75	.408	.122
	10.25	.366	.122
	10.75	.324	.082
	11.25	.268	.082
	12.00	.211	.041
	12.75	.197	.020
	13.25	.183	.020
	13.75	.169	.000
	14.25	.127	.000
	14.75	.113	.000
	15.25	.056	.000
	16.50	.042	.000
	18.50	.000	.000
MOD.PAP	-1.000	1.000	1.000
	.500	.930	.612
	1.250	.887	.571
	1.750	.775	.388
	2.250	.761	.347
	3.000	.718	.286
	3.750	.634	.245
	4.250	.577	.204
	4.750	.549	.204
	5.250	.507	.184
	5.750	.493	.163
	6.250	.451	.122
	6.750	.423	.122
	7.250	.380	.122
	7.750	.352	.102
	8.250	.338	.102
	9.000	.282	.082

	9.750	.254	.041
	10.250	.197	.020
	10.750	.169	.020
	11.750	.113	.000
	13.000	.056	.000
	14.500	.000	.000
PPI Score	-1.00	1.000	1.000
	.50	.972	.633
	1.25	.676	.306
	1.75	.676	.286
	2.25	.620	.286
	3.00	.507	.245
	3.75	.408	.184
	4.25	.408	.163
	4.75	.352	.122
	5.25	.296	.041
	5.75	.254	.041
	6.25	.211	.020
	6.75	.155	.000
	7.25	.141	.000
	7.75	.127	.000
	8.25	.085	.000
	8.75	.070	.000
	9.75	.056	.000
	11.00	.042	.000
	11.75	.028	.000
	13.50	.014	.000
	16.00	.000	.000
MOD_PPI	-1.00	1.000	1.000
	.50	.986	.653
	1.25	.817	.449
	1.75	.817	.429

	2.25	.789	.408
	2.75	.761	.367
	3.25	.704	.327
	4.00	.676	.286
	4.75	.620	.286
	5.25	.577	.286
	5.75	.549	.265
	6.25	.549	.224
	6.75	.535	.224
	7.25	.479	.184
	7.75	.465	.184
	8.25	.380	.163
	8.75	.366	.143
	9.25	.352	.102
	9.75	.324	.041
	10.25	.310	.041
	10.75	.282	.041
	11.50	.225	.020
	12.25	.211	.020
	12.75	.183	.000
	13.25	.169	.000
	13.75	.155	.000
	14.25	.127	.000
	14.75	.099	.000
	15.05	.085	.000
	15.55	.070	.000
	17.00	.056	.000
	18.25	.042	.000
	19.25	.028	.000
	21.75	.014	.000
	24.50	.000	.000
The test result variable(s): PaP Score, MOD.PAP, PPI Score, MOD_PPI has at least			

one tie between the positive actual state group and the negative actual state group.
a The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

Coordinates of the Curve

Test Result Variable(s)	Positive if Greater Than or Equal To(a)	Sensitivity	1 - Specificity
PaP Score	-1.00	1.000	1.000
	.25	.971	.915
	.75	.971	.898
	1.25	.941	.831
	1.75	.882	.780
	2.25	.882	.729
	2.75	.824	.644
	3.25	.794	.627
	3.75	.735	.627
	4.25	.735	.559
	4.75	.676	.508
	5.25	.676	.458
	5.75	.676	.441
	6.25	.647	.373
	6.75	.618	.288
	7.25	.588	.237
	7.75	.471	.186
	8.25	.382	.169
	8.75	.353	.153
	9.25	.324	.136
	9.75	.324	.102

	10.25	.294	.102
	10.75	.294	.051
	11.50	.235	.034
	12.25	.206	.034
	12.75	.118	.017
	13.25	.088	.017
	13.75	.059	.017
	14.25	.059	.000
	14.75	.029	.000
	16.00	.000	.000
MOD.PAP	-1.000	1.000	1.000
	.500	.882	.712
	1.250	.853	.712
	1.750	.824	.525
	2.250	.765	.458
	3.000	.765	.441
	3.750	.706	.339
	4.250	.618	.305
	4.750	.588	.237
	5.250	.559	.186
	5.750	.559	.169
	6.250	.559	.153
	6.750	.412	.068
	7.250	.382	.051
	7.750	.353	.051
	8.250	.324	.051
	9.000	.176	.017
	9.750	.147	.017
	10.500	.118	.000
	11.500	.059	.000
	12.250	.029	.000

	13.500	.000	.000
PPI Score	-1.00	1.000	1.000
	.50	.853	.678
	1.50	.735	.356
	2.25	.706	.356
	3.00	.618	.254
	3.75	.441	.153
	4.25	.412	.119
	4.75	.353	.119
	5.50	.206	.017
	6.25	.147	.000
	7.00	.118	.000
	7.75	.088	.000
	8.25	.059	.000
	9.75	.029	.000
	12.00	.000	.000
MOD_PPI	-1.00	1.000	1.000
	.50	.882	.780
	1.50	.853	.559
	2.25	.824	.492
	2.75	.824	.424
	3.25	.794	.322
	3.75	.706	.322
	4.25	.676	.322
	4.75	.618	.271
	5.25	.588	.237
	5.75	.559	.203
	6.25	.529	.153
	6.75	.500	.136
	7.25	.412	.119
	7.75	.324	.068
	8.25	.265	.051

	9.00	.265	.034
	10.00	.235	.034
	10.75	.206	.034
	11.50	.147	.017
	13.00	.147	.000
	14.25	.118	.000
	15.25	.059	.000
	16.50	.029	.000
	18.00	.000	.000

The test result variable(s): PaP Score, MOD.PAP, PPI Score, MOD_PPI has at least one tie between the positive actual state group and the negative actual state group.

a The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

ROC Curve

Coordinates of the Curve			
Test Result Variable(s)	Positive if Greater Than or Equal To(a)	Sensitivity	1 - Specificity
PaP Score	-1.00	1.000	1.000
	.25	.971	.907
	.75	.971	.852
	1.25	.933	.750
	1.75	.905	.704
	2.25	.905	.657
	2.75	.838	.583
	3.25	.819	.528
	3.75	.790	.528
	4.25	.752	.444
	4.75	.686	.407
	5.25	.648	.361
	5.75	.619	.352

	6.25	.571	.296
	6.75	.562	.250
	7.25	.543	.222
	7.75	.505	.194
	8.25	.457	.167
	8.75	.438	.148
	9.25	.419	.139
	9.75	.381	.111
	10.25	.343	.111
	10.75	.314	.065
	11.25	.257	.056
	11.75	.219	.037
	12.25	.210	.037
	12.75	.171	.019
	13.25	.152	.019
	13.75	.133	.009
	14.25	.105	.000
	14.75	.086	.000
	15.25	.038	.000
	16.50	.029	.000
	18.50	.000	.000
MOD.PAP	-1.000	1.000	1.000
	.500	.914	.667
	1.250	.876	.648
	1.750	.790	.463
	2.250	.762	.407
	3.000	.733	.370
	3.750	.657	.296
	4.250	.590	.259
	4.750	.562	.222
	5.250	.524	.185
	5.750	.514	.167

	6.250	.486	.139
	6.750	.419	.093
	7.250	.381	.083
	7.750	.352	.074
	8.250	.333	.074
	9.000	.248	.046
	9.750	.219	.028
	10.250	.171	.009
	10.750	.152	.009
	11.500	.095	.000
	12.250	.086	.000
	13.000	.038	.000
	14.500	.000	.000
PPI Score	-1.00	1.000	1.000
	.50	.933	.657
	1.25	.695	.333
	1.75	.695	.324
	2.25	.648	.324
	3.00	.543	.250
	3.75	.419	.167
	4.25	.410	.139
	4.75	.352	.120
	5.25	.267	.028
	5.75	.238	.028
	6.25	.190	.009
	6.75	.143	.000
	7.25	.133	.000
	7.75	.114	.000
	8.25	.076	.000
	8.75	.057	.000
	9.75	.048	.000
	10.75	.038	.000

	11.25	.029	.000
	11.75	.019	.000
	13.50	.010	.000
	16.00	.000	.000
MOD_PPI	-1.00	1.000	1.000
	.50	.952	.722
	1.25	.829	.509
	1.75	.829	.500
	2.25	.800	.454
	2.75	.781	.398
	3.25	.733	.324
	3.75	.686	.306
	4.25	.676	.306
	4.75	.619	.278
	5.25	.581	.259
	5.75	.552	.231
	6.25	.543	.185
	6.75	.524	.176
	7.25	.457	.148
	7.75	.419	.120
	8.25	.343	.102
	8.75	.333	.083
	9.25	.324	.065
	9.75	.295	.037
	10.25	.286	.037
	10.75	.257	.037
	11.50	.200	.019
	12.25	.190	.009
	12.75	.171	.000
	13.25	.162	.000
	13.75	.152	.000
	14.25	.124	.000

	14.75	.086	.000
	15.05	.076	.000
	15.55	.067	.000
	16.50	.048	.000
	17.50	.038	.000
	18.25	.029	.000
	19.25	.019	.000
	21.75	.010	.000
	24.50	.000	.000

The test result variable(s): PaP Score, MOD.PAP, PPI Score, MOD_PPI has at least one tie between the positive actual state group and the negative actual state group.

a The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

Appendix II Format for Obtaining Verbal Consent

We are doing a research study to help us to better understand the clinical course of our patients, based on their physical problems.

If you and your relative are willing, one of our staff will phone once a month to find out about the patient's condition.

For patients who have not had a recent WBC count about 2 ml of blood be taken for these tests.

You and your relative are free to refuse to take part in the study, or to withdraw at any time. If you have any questions regarding the study you may contact Dr Abraham.Phone -9442314682.

- நோயாளிகள் பெறும் சிகிச்சையை இன்னும் நன்றாக புரிந்து கொள்வதற்காக, நோயாளிகள் உடல் சார்ந்த பிரச்சனைகளை அடிப்படையாகக் கொண்டு ஒரு ஆராய்ச்சி செய்கிறோம்.

- இதற்கு நீங்களும் உங்கள் உறவினரும் சம்மதித்தால், எங்கள் பணியாளர் ஒருவர் மாதம் ஒருமுறை தொலைபேசி மூலம் உங்கள் உடல் நிலை குறித்து விசாரிப்பார்.

- அண்மையில் இரத்த வெள்ளை அணுக்களின் எண்ணிக்கை குறித்த சோதனை செய்யாதவர்களுக்கு, அந்த சோதனை செய்வதற்காக 2 மிலி இரத்தம் எடுக்கப்படும்.

- இந்த ஆராய்ச்சியில் பங்கு பெற மறுக்கவோ அல்லது எப்போது வேண்டுமானாலும் இதிலிருந்து விலகவோ செய்யலாம்.

- இது குறித்து உங்களுக்கு ஏதாவது சந்தேகம் இருந்தால் நீங்கள் Dr.ஆபிரகாம்-ஐ தொடர்புகொள்ளலாம் (அலை பேசி எண் : 9442314682)

Appendix III - EAPC RecommendationsR

Recommendation 1

In advanced cancer patient management, physicians should base their decisions about therapeutic interventions and settings of care considering both

quality of life and life expectancy (grade D)

An accurate prognostication of life expectancy will facilitate decision making both for professional careers and for patients and their families (grade D)

Recommendation 2

The clinical prediction of survival is a valid tool to obtain a general prognostic evaluation of patients (grade A), but it is subject to a series of factors

that limits its accuracy (see text); its use is recommended together with other prognostic factors (grade A)

Recommendation 3

Clinicians can use a number of clinical signs and symptoms that have proven to be associated with life expectancy in this patient population:

performance status (grade B), cancer anorexia-cachexia syndrome signs and symptoms (grade B), dyspnea (grade B), and cognitive failure or

delirium (grade B)

Recommendation 4

Clinicians can use some laboratory variables associated with life expectancy: leukocytosis (grade B), lymphocytopenia (grade B), and high C-reactive protein (grade B).

The need for a blood sample should be balanced with the clinical advantage that is envisaged and never taken lightly (grade D)

Recommendation 5

Clinicians can make use of some easily applicable prognostic scores to make a rapid prediction capable of identifying classes of patients with significantly different life expectancies (grade A)

At the moment, the Palliative Prognostic Score is the more readily available system including most of the factors (grade A)

Recommendation 6

Establishing a prognosis is part of the therapeutic alliance; patients have the right to be informed or not to be informed about their prognosis

Using and communicating prognostic information should be within the context of a comprehensive, individualized, patient-centered approach

Appendix IV The Karnofsky and ECOG Performance Status Scales and Palliative Performance Scale (PPSV2)

PERFORMANCE SCALE		PALLIATIVE					
KARNOFSKY PERFORMANCE STATUS SCALE	EASTERN COOPERATIVE ONCOLOGY GROUP PERFORMANCE STATUS	PPS LEVEL	AMBULATION	ACTIVITY AND EVIDENCE OF DISEASE	SELF-CARE	INTAKE	CONSCIOUS LEVEL
100%:Asymptomatic 90%: Few signs or symptoms 80%: Normal activity, more signs and symptoms 70%: Capable of self-care but not normal activity 60%: Capable of most selfcare, requires help with some activities 50%: Requires frequent assistance and medical care 40%: Disabled 30%: Severely disabled,hospitalization indicated 20%: Very sick, urgently requiring hospitalization 10%: Moribund	0: Asymptomatic 1: Symptomatic but capable of full self-care, ambulatory 2: Symptomatic, in bed or chair <50% of the time;not able to work 3: In bed or chair >50% of the time, not bedbound,but requires assistance with some ADL 4: Bedbound 5: Dead	100%	Full	Normal activity and work; no evidence of disease	Full	Normal	Full
		90%	Full	Normal activity and work; some evidence of disease	Full	Norma	Full
		80%	Full	Normal activity with effort; some evidence of disease	Full	Normal or reduced	Full
		70%	Reduced	Unable to do normal job/work; significant disease	Full	Normal or reduced	Full
		60%	Reduced	Unable to do hobby/ house work; significant disease	Occasional assistance necessary	Normal or reduced	Full or confusion
		50%	Mainly sit/Lie	Unable to do any work; extensive disease	Considerable assistance required	Normal or reduced	Full or confusion
		40%	Mainlyin bed	Unable to do most activity; extensive disease	Mainly assistance	Normal or reduced	Full or drowsy +/- confusion

0%: Dead		30%	Totally bed bound	Unable to do any activity; extensive disease	Total care	Normal or reduced	Full or drowsy +/- confusion
		20%	Totally bed bound	Unable to do any activity; extensive disease	Total care	Minimal to sips	Full or drowsy +/- confusion
		10%	Totally bed bound	Unable to do any activity; extensive disease	Total care	Mouth care only	Drowsy or coma,+/- confusion
		0%	Death				

Appendix V-Proforma

Name :
Hospital number:
Consent : Yes/ No
Diagnosis:

Contact person name :
Telephone number:
Follow up: Yes/ No

PaP score

Score	Prognostic variable	
0	**Dyspnoea** Absent	
1	Present	
0	**Anorexia** Absent	
1.5	Present	
0	**Karnofsky performance status** ≥ 50 (ECOG 0,1,2)	
2.5	10-40 (ECOG 3,4)	
0	in weeks >12	
2	11-12	
2.5	7-10	
4.5	5-6	
6	3-4	
8.5	1-2	
0	Total white blood cell count Normal(4800-8500) cell/mm^3	
0.5	High (850-11 000) cell/mm^3	
1.5	Very high (>11 000) cell/mm^3	
0	Lymphocyte % Normal (20%-40%)	
1	Low (12%-19.9%)	
2.5	Very low (0%-11.9%)	

PPI

Score	Variable	
4	**Palliative performance scale** (modified Karnofsky) 10-20 (ECOG 4)	
2.5	30-50 (ECOG 3)	
0	≥60 (ECOG 0,1,2)	
2.5	**Oral intake** Severely reduced	
1.0	Moderately reduced	
0	Normal	
1.0	**Oedema** Present	
0.0	Absent	
3.5	**Dyspnoea at rest** Present	
0.0	Absent	
4.0	**Delirium** Present	
0.0	Absent	

Interpretation of the PaP score

Group	Total score
A	0-5.5
B	5.6-11
C	11.1-17.5

Interpretation of PPI

Group	Total score
A	<=4
B	> 4 and < or = 6
C	> 6